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TRANSLATED BY

GEORGE E. DAY, M.D., F.R.S.

FELLOW OF THE ROYAL COLLEGE OF PHYSICIANS, AND PROFESSOR OF MEDICINE IN THE UNIVERSITY OF ST. ANDREWS.

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MDCCCLIII.

AUTHOR'S PREFACE.

NOTWITHSTANDING my earnest desire to include the whole of my materials in the present volume, I have been compelled to devote it exclusively to the Animal Juices, and to postpone the chemistry of the animal tissues and organs, and the consideration of the zoo-chemical processes, to a third volume. In discussing the chemical characters and the composition of the animal tissues, I shall include the recent investigations regarding the parenchymatous fluids of the animal body. Liebig's examination of the juice of flesh has afforded an admirable model, which has already stimulated other chemists to pursue similar courses of inquiry. The third and concluding volume, which will appear in the course of the present year, will embrace Histo-Chemistry and Zoo-Chemical Processes generally, with especial reference to Digestion, Respiration, and Nutrition.

LEIPSIC,
July, 1850.

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TABLE OF THERMOMETRIC DEGREES.

C.		F.	C.		F.
10°	=	50°	40°	=	104°
12		53·6	60		140
15		59	90		194
20		68	100		212
30		86	120		248
35		95	145		293
37		98·6	187		368·6

ADDITIONAL ERRATA IN VOL. I.

Page 12. In the Table of Thermometric Degrees, *for* "10° C=54·5 F" *read* "10° C=50° F;" *for* "145° C=116° F" *read* "145° C=293° F; and *for* "155° C=11° F" *read* "155° C=311° F."

Page 44, line 22 from top, *for* "Hydrogen" *read* "Oxygen."

Page 218, line 4 from top, "he never operated on less than two pounds of blood." Lehmann has here fallen into the error of mistaking grains for grammes. Garrod states, in his Memoir in the 31st volume of the Medico-Chirurgical Transactions, that he usually employed 1000 grains of serum, which is equivalent to about two fluid ounces. I am assured by him, that in no instance has he caused the abstraction of more than six ounces of blood from gouty patients, and in most cases the quantity did not exceed three or four ounces.—G. E. D.

Page 393, line 7 from the top, *for* "fluids" *read* "solids."

PHYSIOLOGICAL CHEMISTRY.

ANIMAL JUICES.

In our methodological introduction to physiological chemistry, (see vol. i. pp. 12—14), the position was indicated which the theory of animal juices occupies, as an intermediate link between the theory of the organic substrata and that of the zoo-chemical processes; while the point of view was likewise defined from which this branch of physiological chemistry ought to be considered. It therefore only remains for us to make a few remarks on the mode of arrangement adopted in the following chapters, before proceeding to the special consideration of our subject. We purpose following in the main the same mode of arrangement which we endeavoured to pursue in treating of the organic substrata in the first volume; that is to say, we shall begin the notice of each object by considering its physical and chemical characters. The *mode of preparation* seems at first sight a matter of little moment, since these substances are usually submitted to examination in the condition in which they are directly yielded by nature. But although the exhibition of such objects does not require the aid of chemistry, we may often find it difficult to command the mechanical and physiological means requisite for procuring the substance in a pure condition, that is to say, unmixed and undecomposed. The result of the whole chemical operation is often dependent on the manner in which the object is exhibited, and it will be found that an unsuitable method of exhibition frequently leads to the adoption of wholly erroneous views in reference to the nature and function of an animal fluid. It is only when we are convinced that the animal fluid is presented to us in the same state in which it exists in the living body, that we can hope to obtain any physiological result from our investigation. As the exhibition of many animal fluids, moreover, frequently requires that the experimentalist should be familiar with certain anatomico-surgical operations, we think it will hardly be deemed superfluous, if we consider the methods adopted for procuring some of the animal juices.

When we have obtained a physiologically pure substance, studied its physical characters, and determined by the microscope the presence or absence of morphological elements, we must next consider the method in which the *chemical analysis* should be conducted. It is obvious that the plan and method of the analysis may vary in accordance with the special aims of the investigation, and will in general depend upon the nature of the constituents of the fluid. We have therefore thought it expedient to indicate the analytical methods of analysis suited to the different fluids. But as we are still on the very threshold of the enquiry, we can do no more than present the rudiments of a future organic analytical chemistry. As we have already observed in the first volume, physiological chemistry, considered as an inductive science, requires most especially to be based on exact principles amenable to calculation. Unfortunately, however, all chemists concur in admitting that a large number of analyses of the animal fluids rank among the most slovenly and unprincipled investigations of their science. How many of these show at the first glance that they are utterly worthless! In such a state of things it will scarcely be deemed superfluous to specify some few of the properties which it is necessary for the analysis to possess in order to render it of any value in a scientific point of view.

As we have already referred in the first volume to the qualitative and quantitative determinations of the individual animal substrata, it only remains for us to observe, in reference to compound fluids generally, that in the *qualitative* analysis of the animal juices, the largest possible quantity should be employed—a point the importance of which was first fully demonstrated by Liebig's investigations regarding the juices of the flesh, &c. For *quantitative* zoo-chemical analyses, however, the converse rule holds good, more especially in analyses of the blood. We generally find that too large a quantity has been employed for the determination of the individual constituents in the majority of the blood-analyses on record. As a general rule, it may be asserted that quantitative analyses of the blood and of similar fluids, are the less exact in proportion to the quantity of the substance analysed. This depends partly on the difficulty frequently experienced in passing animal fluids, even when diluted, through a filter, partly on the readiness with which many of the constituents are decomposed, but principally on the impossibility of perfectly and uniformly drying large quantities. In order to avoid as much as possible these and other impediments, we must only employ small quantities of the object in our analysis.

Notwithstanding every care and precaution, difficulties will however present themselves in the analysis of animal substances, which may escape even the closest attention; and hence, more than in the analysis of any other substances, it is absolutely necessary to institute a rigid *controlling comparison* of the various results, and even a partial repetition of them. Since the same quantity of an animal fluid serves for the determination of only a few of its constituents, our means of controlling the analysis are increased in proportion to the number of determinations made independently of each other. Thus, for instance, in seeking to ascertain the amount of coagulable matters contained in a fluid, the analysis should always be controlled by extracting the solid residue of the fluid with alcohol, ether, and water, and then comparing the quantity of the insoluble matters with the number representing the protein-body determined by coagulation. Thus too, ash-analyses should always be controlled by comparing the mineral constituents of the individual extracts with those of the collective ash. A perfect coincidence would certainly prove the inaccuracy of the analysis in both these cases; for the coagulated substance, unless it has been expressly deprived of its fat, still contains fat, and sometimes even other substances soluble in alcohol but not in water, and which, on the other hand, cannot occur in that portion of the solid residue of the fluid extracted with alcohol and ether, and insoluble in water; for this must always contain more earthy salts than the albumen that has been completely coagulated by the addition of a weak acid. In like manner the analysis of the collective ash cannot coincide with that of the individual extracts, since, for instance, the sulphur contained in the coagulable matters is unable to exert a metamorphic action on the soluble salts of the extracts, whilst the composition of the combined ash must be altogether different, partly on account of the sulphuric acid formed from the unoxidised sulphur of the protein-bodies, partly from the difficult combustion of albuminous substances, and partly from other causes. Although this method may not afford any strict means of controlling these relations, it furnishes a more correct view of the true nature of the substances dissolved in the fluid. This is, to a certain degree, a physiological check; but it would be superfluous to indicate any special methods of control, since every analysis of an animal fluid, and even almost every individual determination, admits of being tested by the most rigid purely chemical checks. We shall find that these controlling or controlled analyses frequently afford the most unexpected proofs of the value of the method of analysis, by the light they throw upon the true constitution of the object under examination.

C. Schmidt* has employed an ingenious and original method for ascertaining the correctness of the complete analysis of an animal fluid; it consists in comparing the empirically found specific weight, with the sum of the specific weights of the individual constituent parts, according to the proportions yielded by the analysis. Such a controlling calculation of the density cannot of course be based upon the specific weights of the dried substances and of the water; since all substances when dissolved in water undergo a condensation with it. It is a highly important circumstance in relation to the complete physiological consideration of the animal fluids and of the mechanical metamorphosis of matter, that the dissolved substances do not occur, as has been generally supposed, in a mere condition of mechanical distribution and admixture, but that when dissolved in different quantities of water, they enter into different hydrate-like combinations with that fluid, and consequently exhibit various degrees of condensation. Schmidt has determined the coefficients of condensation for the ordinary constituents of animal fluids, and made the density of the solutions which contain exactly 10% of solid substances (at + 15° C. in vacuo) the basis of his controlling check. Knowing the relations of the individual constituents from the analysis, we may easily calculate the specific gravity of the collective fluid from the sum of the coefficients of condensation, and may then compare it with the empirically found specific gravity.

The following illustration will serve to elucidate the table compiled by Schmidt for the purpose already stated. The specific gravity of chloride of sodium (at + 15° C. in vacuo) is = 2·1481; hence, if the salt in a solution containing 10% of chloride of sodium were distributed in the water without condensation, this solution would have a specific gravity of 1·0565; for 10 parts of dry chloride of sodium (its specific gravity being = 2·1481) occupy the space of 4·655 parts of water; with 90 parts of water, therefore, the solution should occupy the space of 94·655 parts of

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* Characteristik der Cholera. Mitau, 1850, S. 22—28.

water; but when we examine the specific gravity of such a solution, we find that it is higher, that is to say = 1·0726. In accordance with this density, ten parts of chloride of sodium and ninety parts of water, occupy only the space of 93·231 parts of water; hence a condensation of 1·424 parts must have taken place; for every 100 volumes there would, therefore, be a condensation of 1·505 volumes between one part of chloride of sodium and nine parts of water. With these preliminary remarks we proceed to give Schmidt's table.

Substance.	Density of the solution containing 10$^0_0$ of solid substance.	Density of the dry substance.	Per centage, according to volume, of the condensation occurring in the solution containing 10$^0_0$.
Chloride of sodium	1·0726	2·1481	1·505
Chloride of potassium	1·0653	1·9787	1·348
Sulphate of potash	1·0833	2·6616	1·541
Phosphate of potash, 2 KO.PO$_5$	1·0960	2·4770	2·974
Phosphate of soda, 2 NaO.PO$_5$	1·0994	2·3735	3·455
Potash	1·1001	2·6560	3·035
Soda	1·1484	2·8050	6·933
Phosphate of lime, 3 CaO.PO$_5$	1·0807	3·0976	0·744
Phosphate of lime, 2 CaO.PO$_5$	1·0896	3·0596	1·600
Phosphate of magnesia, 2 MgO.PO$_5$	1·0913	3·0383	1·776
Phosphate of iron, Fe_2O_3 PO$_5$	1·0880	3·0661	1·447
Urea	1·0275	1·3369	0·160
Glucose, C_{12} H_{12} O_{12}	1·0396	1·3860	0·766
Fibrin	1·0270	1·2858	0·420
Albumen	1·0268	1·2746	0·426

We forbear offering any remarks in this place on the interesting points of view which are opened to us by Schmidt's admirable investigation, as we must return to the full consideration of this subject when we treat of the mechanical metamorphosis of tissue.

Schmidt employs specific gravities as a check on analyses, in the following manner. The analysis of a specimen of serum, whose specific gravity was found to be 1·0292, gave 82·59 p.m. of organic constituents, 0·283 p. m. of sulphate of potash, 0·362 of chloride of potassium, 5·591 of chloride of sodium, 0·273 of phosphate of soda, 1·545 of soda, 0·300 of phosphate of lime, and 0·220 of phosphate of magnesia. The following is the manner in which the check is applied:—

82·586	grammes	of albumen with extractive matters (the condensation dependent on solution being allowed for)	fill the space of	61·471	of water.
2·836	,,	of the 10% solution of sulphate of potash	,,	2·618	,,
3·616	,,	,, chloride of potassium	,,	3·395	,,
55·914	,,	,, chloride of sodium	,,	52·129	,,
2·726	,,	,, phosphate of soda	,,	2·480	,,
15·454	,,	,, soda	,,	13·457	,,
2·997	,,	,, phosphate of lime	,,	2·773	,,
2·197	,,	,, phosphate of magnesia	,,	2·013	,,
168·326	grammes	of the collective solution	,,	140·336	of water.

Hence we calculate the density of serum, having this composition, to be 1·0288; for 140·336 : 168·326 :: 1 : x (= 1·0288).

After having acquainted ourselves with the chemical constitution of the animal juices in their normal state, we have next to consider the modifications experienced by the fluids in question under *different physiological and pathological relations*, considering at the same time the composition of the corresponding juices in different classes of animals. The latter indeed constitutes the most common subject of our physiologico-chemical inquiries, and the main basis of our investigations.

Before we consider the *pathological* relations, it will be necessary to make a few preliminary remarks. What we have already said in the first volume in reference to the mode of treating of pathological chemistry, sufficiently demonstrates how visionary are all anticipations of the formation of a perfect humoral pathology, which indeed is a science that has no existence except in the dreams of mere enthusiasts. According to the principles on which we would base our consideration of pathological processes, we cannot group the physical and chemical alterations observed in animal juices within the generally recognised classes of disease, but must arrange them in harmony with the internal, that is to say, the chemical constitution of the pathological objects. It seems to us, that we should be assuming an entirely false point of view, were we to start from conventionally named diseases, as tuberculosis, carcinoma, &c. Notwithstanding the frequent objections advanced against the ontological modes of definition in use for diseases, an entirely specific character has nevertheless been ascribed to these hackneyed designations of certain forms of disease, since otherwise the idea that tubercles are mere depositions of exudation, and similarly erroneous notions, could never have become current. That we may avoid such a fictitious species of physiology, we shall adhere as strictly as possible to the object itself, merely reverting, where it is absolutely necessary, to its conventional predicate.

Although we may describe the bile in the dead body as poor in solid constituents after violent inflammations, as still thinner and more watery in typhus, and sometimes deficient and at other times abundant in solid constituents in tuberculosis, we must, nevertheless, consider this designation of the conditions in which the bile is found to be more concentrated or more attenuated, as wholly irrational; for we ought simply to have said that in those conditions in which, to borrow an expression from pathological anatomy, the morbid process had localised itself, or, in other words, where the blood had lost some of its solid contents, in consequence of extensive exudations or other considerable losses of the juices, this property of the blood was reflected as it were in the secretions and excretions, and a less consistent and poorer bile was secreted; whilst in those cases in which the blood is found to be denser and to contain more solid constituents, as for instance in cholera, the bile in the body after death is viscid and deficient in water.

Another point of physiological importance in relation to the animal fluids, is the investigation of the quantities in which they are *formed or secreted*, and this is far more necessary than we should be disposed at first sight to infer. We have already shown, in our methodological introduction, the importance to be attached to the statistical method of examining the metamorphosis of matter, and recognised it as one of the most valuable aids in physiologico-chemical investigation, for, although it still leaves us in the dark as to the nature and objects of such a process, it defines certain boundaries beyond which we cannot strain our interpretation of animal phenomena, or extend our experiments, without falling into the most obvious errors. Such a limitation of hypotheses is above all most necessary in a science which may still be said to be in its infancy. The benefits derived from this statistical method are not, however, merely negative; for it affords the surest basis for the recognition of that branch of physiological chemistry which promises to yield the richest fruits to future inquirers. The most direct and attainable aim of our investigations must be the elucidation of the quantitative relations of the interchange of the different animal substances through the different organs, tissues, closed and open cavities, and finally, the external world. In the present low state of our knowledge of the chemical substrata of the human organism in health as well as in disease, it is to a development of the mechanical metamorphosis of matter based upon physical laws, and referable to simple numerical calculations, that we must look for the most brilliant results.

The groundless hypotheses of crases and dyscrases stimulated zeal for the chemical investigation of morbid products; but what have we learnt from the innumerable analyses of morbid blood and urine, beyond the fact that the quantitative proportions of the ordinary constituents of these juices have undergone certain modifications? As we have but little chance of success, at least for the present, in seeking for deleterious matters, specific contagia, a materia peccans, &c., we should rather direct our inquiries to the elucidation of the quantitative relations of the substances known to us, and to their distribution in the different animal juices. But a meagre enumeration of the barren results of chemical analyses in per-centage tables is insufficient for this end, since what we require is to bring these results into harmony with the relations of mass existing between the different animal fluids, and with the amount of motion occurring between the juices that are separated by membranes and cells. If, for instance, we compare the quantities of the substances occurring in the secretions during disease with those which remain in the blood, we shall arrive at results yielding the most interesting materials to physiological mechanics, in elucidating the course of morbid processes and the causal connexion existing between entire groups of symptoms, as has been ably shown by C. Schmidt in his admirable investigations on the processes of transudation in cholera, Bright's disease, dysentery, and dropsical conditions. The knowledge of the quantitative relations in which each animal fluid and its individual constituents are formed or secreted, supplies the basis of the statistics of animal molecular motion; we purpose, therefore, entering into a special consideration of the mechanical metamorphosis of matter in the animal organism, in our third volume, where we shall further endeavour to reconcile the results of the quantitative physiologico-chemical inquiries with the theories of the imbibition of animal membranes, of endosmosis, and of the transudation depending upon the elasticity and thickness of the membranes as well as upon the rapidity of the motion of the blood. Without such points of support, based on physical laws and arithmetical conclusions, few hypotheses regarding nutrition and secretion, and the metamorphosis of the body generally, can attain any degree of logical accuracy. We have therefore regarded it as perfectly falling within the province of physiological chemistry to give the quantity of the matters secreted, and the amount of chemical motion of each animal juice, as far as the state of science enables us to form such estimates.

A larger portion of the systematic treatment of the animal juices will be devoted to a consideration of the *metamorphoses* experienced by each separate object within the living animal organism, and the changes and decompositions observed in the same substance external to the sphere of vitality. If we subjoin, as in our notice of the animal substrata, those circumstantial data which can alone justify us in considering the *genetic* development of each object, we shall be in possession of all the elements, as far as the present state of science permits, for forming an opinion regarding the *function* or *physiological value* of every individual animal fluid. By such a course, we shall certainly be carried within the province of physiological processes; but in considering the metamorphosis of animal matter generally, and the processes of digestion, respiration, and nutrition, in their systematic connexion, our views of the chemistry of the animal body should not be diverted to individual points, but rather be made to combine with the conclusions obtained by simple induction, in reference to the function of the individual chemical agents. (See Vol. I. p. 3.)

If ever we cherished the hope of combining the results of former inquiries into one scientific whole, constituting a purely inductive branch of science, in accordance with our view of the method in which physiological chemistry, and more especially the theory of the animal juices, should be treated, our courage would fail, as indeed it often has done, when we attempted the accomplishment of such a task. We believe that, in the first volume, we have already sufficiently explained our view of the very great deficiency of our knowledge in this department of the physical sciences; but here it is less a want of positive knowledge than a redundancy of materials that renders it a matter of almost insurmountable difficulty to demonstrate with clearness the pure and unadulterated character of science free from pretentious delusions. A cursory glance at the confused mass of materials accumulated before us, presents a view of disorder requiring Herculean efforts to disentangle them. We confess that we have therefore abstained from attempting in the following pages to give the whole mass of the results that have been obtained within this department of science from all experiments and observations, whether good or bad; limiting ourselves to facts collected by the best observers, which, as far as our powers and experience permitted, we have compared with the results of our own observations, testing the different conclusions and hypotheses by a course of logical inquiry. Without reference to the present work, which we have designated as a mere attempt, in genuine sincerity, and apart from all pretended modesty, it will not be denied that far greater service will be done to the theory of animal juices as well as to physiological chemistry, by an experimental criticism, than by the most careful collection of all that bears upon the subject in literature. In our attempt to sift the rich mass of materials presented to our notice, we shall endeavour to abstain from all mere polemical criticism, and adhere to facts only, which must ever constitute the only solid support of natural science.

Saliva.

The saliva discharged from the mouth is not merely a mixture of the fluids secreted by the different salivary glands, but also contains, as an essential constituent, the buccal mucus, or the secretion of the mucous membrane of the oral cavity. The mixed or ordinary saliva is therefore by no means identical with the secretions of the different salivary glands, from which it differs both in its chemical characters and in its physiological action.

The *mixed saliva* of man and of most of the mammalia exhibits the following properties: it occurs as a rather turbid, opalescent, or faintly bluish white fluid, which is somewhat viscid and capable of being drawn out in threads, and is devoid of odour and taste. After standing for some time, it deposits a mucous greyish white sediment, which, when examined under the microscope, is found to consist chiefly of pavement epithelium, often united so as to form shreds, and what are termed mucus-corpuscles, which are usually a little larger than pus-corpuscles, and generally exhibit a large, lenticular, excentric nucleus, even without the application of any special re-agents. The specific gravity of mixed saliva is liable to variations even in the normal state; for its density is partly dependent on the quantity of mucus that may be mixed with it, and partly on the greater or less attenuation of the glandular secretion; its usual variations in man are between 1·004 and 1·006; it may, however, in the normal state rise to 1·008 or 1·009, or, on the other hand, it may sink to 1·002. Normal saliva presents a more or less distinctly alkaline reaction: it has no poisonous effect either on plants or animals.

There is scarcely any animal fluid in which it is of such importance that the specimen we are examining should be perfectly fresh; for none becomes so rapidly changed and so soon completely decomposed as the saliva. A disregard of this fact is the cause of many of the errors which have led to the most remarkable views regarding the saliva. It is thus, probably, for instance, that Wright* has ascribed to this secretion many properties which have either not been at all noticed by other observers, or at all events in a less degree. We may refer, by way of example, to the taste of the saliva, which, according to Wright, is "sharp, saline, and slightly astringent,"—a statement which I must agree with Jacubowitsch† in totally denying; for, in opposition to Wright's assertion, I have always found the saliva of healthy persons to be tasteless. The injurious action of saliva on vegetable and animal organisms, which has been observed and described by Wright, depends for the most part, as may be shown by positive experiments, on the fact of its not being perfectly fresh.

The morphological elements of the saliva owe their origin to the mucous membrane of the buccal cavity, and in a lesser degree also to that of the salivary ducts; hence, these bodies will be described in the chapter on "Mucus." In examining expectorated saliva we sometimes find not only epithelium and mucus-corpuscles, but also fat-globules, and occasionally the remains of food, as, for instance, vegetable cells or beautifully macerated muscular fibre, and still more rarely vibriones, which take their origin in mucus or fragments of food retained for a long time between the teeth, or in hollow carious teeth.

The presence of *mucus-corpuscles* in normal saliva or the buccal mucus has been called in question, and it has been asserted that they only occur after some slight irritation of the mucous membrane of the mouth, as, for instance, after smoking tobacco; but I have always been able to detect some of them in the buccal mucus of healthy persons (even of such as are not in the habit of smoking); and as they likewise occur in the saliva of animals, as for instance, of dogs and horses (Magendie,‡ Jacubowitsch§), it cannot be doubted that the buccal mucous membrane, even in its perfectly normal state, throws off these mucus-corpuscles with the epithelial plates, the former indeed being nothing more than abortive epithelial cells.

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* On the Physiology and Pathology of the Saliva. Lancet, 1842.

† De Saliva, diss. inaug. Dorpati, Liv. 1848, p. 12.

‡ Compt. rend. T. 21, p. 905.

§ Op. cit. p. 16.

The extreme variability of the *specific gravity* of the saliva of even the same person, under different physiological relations, may be easily demonstrated by a few experiments. I made some experiments in reference to this point with the parotid secretion of a horse, in whom an artificial salivary fistula was established, by exposing and opening the duct of Steno. Very shortly after the operation the parotid saliva had a density of 1·0061; ten minutes afterwards, when the animal had drank about six pounds of water, and had eaten some hay, the density sank to 1·0051; after having nothing to drink for twelve hours, a feed of hay caused a free secretion of saliva, whose specific gravity was as high as 1·0074. Wright has pointed out that human saliva is denser after food has been taken than in a fasting condition. He found that the saliva of a healthy man who had lived for a week on a mixed diet, varied in its density from 1·0079 to 1·0085; while, after a purely animal diet for an equal time, it varied from 1·0098 to 1·0176; and, after a purely vegetable diet, from 1·0039 to 1·0047. According to this author, moral emotions, atmospheric changes, light, sound, &c., exert an influence on the density of the saliva. From numerous experiments made on 200 healthy persons, he found that the specific gravity of the saliva varied between 1·0089 and 1·0069, a result which is far higher than I have obtained from my experiments. It is possible that the more abundant use of an animal diet amongst the English may have caused the higher density which was found by Wright.

In relation to the *alkalinity* of the saliva, any one may readily observe for himself that, during and after eating, the alkaline reaction increases, while during fasting it very much diminishes, or altogether disappears; indeed, in some persons who are apparently healthy, the saliva during fasting has a weak acid reaction, although immediately after the use of solid food it again becomes alkaline. (Hünefeld*, Mitscherlich†, Wright, Jacubowitsch.) According to Wright, the quantity of soda in the saliva of healthy men varies between 0·095 and 0·353%; in that of dogs between 0·151 and 0·653%; in that of sheep between 0·087 and 0·261%; and in that of horses between 0·098 and 0·513%. We only record these numbers in order to give an approximate measure of the quantity of acid which may be saturated by the saliva; for these numbers are calculated for soda, while in the saliva of graminivorous animals there is often much potash, and always a large quantity of lime which is

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* Chemie und Medicin. Berlin, 1841, S. 43—60.

† Pogg. Ann. Bd. 27, S. 320—347.

expelled from its combination with non-acid organic substances by the very weakest acids, and as for instance even carbonic acid. Frerichs* found that 100 grammes of saliva, secreted by a man smoking tobacco, were neutralized by 0·150 of a gramme of sulphuric acid.

According to Wright, the quantity of alkali in the saliva is increased after the use of fatty, aromatic, acid, spirituous, and more particularly indigestible kinds of food and drink.

In attempting to collect *pure* human saliva, we must avoid the use of irritants—such as tobacco, either smoked or chewed, or aromatics—which, although they increase the secretion, become mixed with it, and render it comparatively unfit for examination. The simplest method of collecting a large quantity of saliva in a short time, is by exerting strong pressure under the chin, and at the same time tickling the palate with a feather; a feeling of strangulation rapidly ensues, during which the saliva is ejected from the mouth. The best method of collecting the saliva of animals, is by presenting them with their favourite food after they have been kept for some time fasting; the secretion flows freely on pressing the nostrils in a backward direction.

The method which Magendie and Lassaigne adopted for the purpose of collecting the mixed saliva of animals, namely, cutting into the œsophagus, cannot be avoided for certain experiments, but, for ordinary purposes, it is not only cruel and indirect, but also unphysiological; for how can we expect, that after such an inroad on animal life as must arise from the exposure and opening of the œsophagus, a secretion can remain in its normal state?

We have already mentioned that ordinary saliva is a mixture of the secretion of the buccal mucous membrane and of several glands; we now proceed to notice these secretions individually.

PAROTID SALIVA has hitherto only been accurately examined in man by Mitscherlich† and Van Setten; the parotid secretion of horses and dogs has, however, very often been analysed. It is usually perfectly limpid and colourless, devoid of smell and taste, incapable of being drawn out in threads, and of a distinctly alkaline reaction. In a male patient, Mitscherlich found that the specific gravity varied from 1·0061 to 1·0088; in dogs it was found by Jacubowitsch to vary from 1·0040 to 1·0047; and in horses I found it to range from 1·0051 to 1·0074.

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* Wagner's Handwörterb. d. Physiol. Bd. 3, Abt. 1, S. 760.

† Op. cit.

‡ De Saliva ejusque vi ut utilitate. Groning. 1837.

The observations of Mitscherlich on the parotid saliva of a man suffering from chronic disease, show that prolonged hunger or the use of indigestible and stimulating food. causes the secretion of a concentrated saliva. Moreover, this observer found that in the fasting state it was always acid, and that it was only alkaline during meals. Magendie and Rayer perceived a gradual diminution in the specific gravity of the parotid saliva of a horse in whose Stenonian ducts fistulous openings had been established.

In regard to the chemical constituents of the parotid saliva, it may be observed that the results of those who have experimented on the subject, do not altogether coincide, probably from their having operated on the saliva of different classes of animals. The following may, however, be regarded as constant ingredients of this secretion:—

(*a*) *Potash*, *soda*, and *lime*, combined with an *organic matter:* this compound is one of the most important of the constituents of the saliva, being that on which several of the properties of this fluid are dependent; it is similar to, but not identical with, albuminate of soda, and corresponds in part to the ptyalin of Berzelius and others.

Magendie, Jacubowitsch, and others, assume that alkaline carbonates are present in the saliva, but their quantity must be extremely small in the fresh secretion; the alkaline carbonates are produced during the different steps of the chemical analysis, by the access of atmospheric air. The formation of carbonate of lime is extremely evident when the parotid secretion of the horse is exposed to the air, for, like lime-water, it attracts carbonic acid, and most beautiful microscopic crystals of carbonate of lime are deposited. The organic matter, the ptyalin, is difficult of solution, although not absolutely insoluble, in water, after its separation from the alkalies or from lime, by carbonic or some other acid; hence human saliva, and that of the dog, is sometimes rendered turbid, and is sometimes apparently unaffected by acids; the precipitate consists of amorphous flocculi, which are difficult of solution in pure water, but dissolve readily if an alkali or an acid be added. We find this substance in part still combined with an alkali, both in the aqueous and in the spirituous extracts; it may be obtained in the greatest purity from the latter, after extraction with alcohol and ether. It then forms an almost gelatinous, colourless substance, which is more or less insoluble in water, according as the alkali has been more or less thoroughly removed by carbonic acid, or some other means. The alkaline solution of this substance yields, on the addition of a little acetic or nitric acid, a flocculent precipitate, which dissolves freely in an excess of acetic acid; when boiled with hydrochlorate of ammonia, or with sulphate of magnesia, the alkaline solution of ptyalin becomes strongly turbid. The alkaline (but not the neutralised) solution of this substance is precipitated by tannic acid, corrosive sublimate, and basic acetate of lead, but not by alum or sulphate of copper. The acetic acid solution becomes strongly turbid on the addition of ferrocyanide of potassium; when boiled with nitric acid, this substance forms a yellow solution. In these respects, it is very similar to albuminate of soda, and to casein, but it must by no means be confounded with them. I have principally studied the properties of this substance in cases in which it had been obtained from the parotid saliva of the horse, and I have arrived at the conclusion, that the differences observed by Berzelius, Gmelin, and others, in reference to ptyalin, may be easily explained. In no other animal fluids could I recognise a substance perfectly identical with this ptyalin.

It is singular that Magendie, in his investigations regarding the parotid saliva, has overlooked the circumstance that it abounds in lime (and assumes only the presence of bicarbonate of potash); while Jacubowitsch* constantly found carbonate of lime in the parotid saliva of dogs. It is possible that differences of food may exert the same influence on the saliva as they do on the urine of horses; for, as we shall subsequently show, the urine of these animals sometimes abounds in carbonate of potash, and sometimes in carbonate of lime; but whenever I analysed the saliva of the horse, I always found it very rich in lime.

(*b*) An *extractive matter* soluble in *alcohol* and in water, which is precipitable by tannic acid, but not by alum.

(*c*) *Sulphocyanide of potassium*, whose presence has been detected by Mitscherlich, Jacubowitsch, and Gmelin, in the parotid saliva of man, the dog, the horse, and the sheep.

I have not observed any reddening on the addition of perchloride of iron to the parotid secretion of the horse.

(*d*) The *potash-salt* of a not very volatile acid belonging to the *butyric acid* group (caproic acid?); it crystallises in a beautiful efflorescent form, which, under the microscope, resembles the tufts of margaric acid.

(*e*) A little *epithelium*, and some scattered *mucus-corpuscles.*

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* Op. cit. p. 20-22.

(*f*) The *chlorides of sodium* and *potassium.*

(*g*) *Phosphates,* in very small quantities.

(*h*) A trace of *alkaline sulphates.*

The following statements may suffice in reference to the *quantitative* relations of the constituents of the parotid secretion: in the parotid saliva of man, Mitscherlich found from 1·468 to 1·632%, and Van Setten 1·62% of *solid constituents;* in that of a dog, Jacubowitsch found only 0·47%, while Gmelin found 2·58%; in that of the horse Magendie found an average of 1·1%; while, as the mean of six experiments with different specimens of saliva, I determined the solid constituents at 0·708%.

In the human secretion, Mitscherlich found nearly 0·525% of *ptyalin* associated with an alkali; in that of the horse, I found on an average 0·140% of pure ptyalin (after the extraction of the mineral substances contained in it).

The alkaline ptyalin obtained from the water-extract and from the spirit-extract insoluble in alcohol, constituted 23·332% of the solid constituents of the saliva of the horse, and yielded 5·675% of ash, which consisted almost entirely of alkaline carbonates and lime.

The *alcohol-extract* of the secretion amounted in man, according to Mitscherlich, to about 0·1%; in that of the horse, I found it amount to 0·0988%.

The alcohol-extract of the saliva of the horse amounted, according to the mean of my experiments, to 13·936% of the solid residue, and yielded 3·812% of ash, consisting chiefly of alkaline chlorides.

No quantitative determination of the *sulphocyanide of potassium* contained in the parotid saliva has yet been attempted.

In the parotid saliva of the horse, I found 0·0403% of a compound of a *fatty acid and potash.*

The ether-extract amounted to 5·703% of the solid residue, and contained 1·102 parts of potash (as determined by bichloride of platinum from the ash).

The *insoluble matter* removed by filtration, and consisting of epithelium with salts, amounted, according to Mitscherlich, to 0·005%, while I found it as high as 0·124% in the saliva of the horse.

The insoluble portion of the saliva of the horse consisted, for the most part, of carbonate of lime; after its abstraction, and that of the ash generally, the insoluble organic matter was very minute; the solid residue contained 17·550$_{\overline{0}}$ of insoluble matters, in which were 13·453 parts of ash; hence the epithelium amounted to only only 4·097% of the whole solid residue.

According to the determinations of Mitscherlich, the solid residue of the parotid saliva in man contains about 45·7% of mineral constituents, in which there are contained 35·4 parts of chloride of potassium, and about the same quality of potash and soda (after deducting the carbonic acid); in this secretion from the dog, Jacubowitsch found that the ratio of the organic to the inorganic matter was as 29·8 : 70·2; the latter consisted of 44·7 parts of alkaline chlorides, and 25·5 of carbonate of lime. In 100 parts of the solid residue of the parotid saliva of the horse, I found 53·9 parts of ash, in which there were 21·764 parts of chloride of potassium, 16·983 of carbonate of potash, and 11·226 of carbonate of lime, while there were only 0·882 parts of the phosphates of lime and magnesia, 0·805 of the sulphate and 2·240 of the phosphate of soda.

The secretion of the submaxillary glands of dogs has been carefully examined by Bernard* and Jacubowitsch; it is, like the parotid saliva, a colourless, limpid, tasteless, and inodorous fluid, and is devoid of all morphological elements. Jacubowitsch determined its specific gravity at 1·0041; the reaction is less strongly alkaline than that of the parotid saliva; it contains far less lime in combination with organic matter, and therefore attracts less carbonic acid from the air than the previously described secretion; in other respects, it contains precisely the same constituents, including the sulphocyanide of potassium. Bernard regards the viscidity of this secretion as constituting an essential difference between it and the parotid saliva, and Jacubowitsch likewise noticed this peculiarity in the submaxillary fluid. According to the last-named observer, it yielded 0·855% of solid residue, in which the ash amounted to 0·566 parts; so that here the ratio of the organic to the mineral constituents was as 33·8 : 66·2; the latter contained 52·6 parts of alkaline chlorides and 13·6 of carbonate and phosphate of lime and magnesia.

Bernard directs attention to the circumstance that an infusion of the parotid gland is very aqueous, and cannot be drawn out in threads, while an infusion of a piece of the submaxillary gland is as viscid as the secretion collected from Wharton's duct.

The secretion of the buccal mucous membrane in dogs has been examined by Jacubowitsch; but the secretions of the orbital and of the sublingual glands (which latter are, however, very little developed in dogs) were mixed with it. This fluid was very viscid and tenacious, frothy, and colourless, but

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* Arch. gén. de Méd. 4 Sér. T. 13, p. 1-29.

extremely turbid from the presence of an enormous number of epithelial cells, which were not deposited when the fluid was allowed to stand. The fluid had an alkaline reaction, and did not coagulate on heating; it left 0·999% of solid residue, in which were 0·385 parts of organic and 0·614 of inorganic matter. The insoluble salts contained no carbonate of lime.

Jacubowitsch collected the mucous secretion of the mouth by tying Steno's and Wharton's ducts, keeping the animal's nostrils open, and retaining the head in an inclined position, so that the animal being unable to swallow, the mucus flowed from the mouth. He collected the secretions of the parotid and submaxillary glands by introducing a fine silver canula into their respective ducts.

In addition to the above-mentioned differences in the individual secretions of which the saliva of the dog is made up, Jacubowitsch further notices that, (*a*) the parotid saliva, exposed to the air, becomes rapidly covered with a film of crystals of carbonate of lime, which is not the case with either of the other secretions; (*b*) that at a temperature of 100°, the parotid saliva does not become turbid, whilst the other secretions, at least in a slight degree, become opaque; (*c*) that the parotid saliva, if boiled with nitric acid, and subsequently treated with ammonia, does not assume the yellow or orange tint which is developed when the secretions of the buccal mucous membrane and the submaxillary glands are similarly treated; and (*d*) that it is only in parotid saliva that carbonate of potash produces a slight precipitation of carbonate of lime.

Jacubowitsch has also analysed the mixed saliva of the dog, in one instance with the exclusion of the parotid, and in another with that of the submaxillary secretion.

After this review of the chemical characters of the different secretions constituting the saliva, we have little to add regarding the composition of MIXED OR ORDINARY SALIVA.

In the ordinary saliva of man, Berzelius* found 0·71% of *solid constituents*, Tiedemann and Gmelin† 1·14 to 1·19%, Wright‡ 1·19%, and L'Héritier§ 1·35%; Jacubowitsch found only 0·484%; Frerichs in 18 analyses, 0·51 to 1·05%; and, from numerous determinations of filtered saliva, I have only found from 0·348 to 0·841%; so that the statements of the older observers are obviously too high.

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* Förelasningar i Diurkemien. 2 vol. Stockholm, 1808.

† Verdauung nach Versuchen, Bd. 1, S. 9 ff.

‡ Op. cit.

§ Chimie pathol. p. 290. Paris, 1842.

In the saliva of the dog Jacubowitsch found 1·037%, and in that of the horse Magendie and Rayer found about 1% of solid residue.

In 100 parts of the solid constituents of mixed human saliva, Tiedemann and Gmelin found 21·3% of fixed salts, while L'Héritier found only 6·8%, and Jacubowitsch, on the other hand, 37·5%; the last-named observer found that the mineral constituents predominated very much in the saliva of the dog, where they amounted to 65·5% of the solid residue; in the horse, according to Magendie, they amounted to 40%.

In relation to the individual *mineral constituents* of the saliva, we are as little able to arrive at any definite conclusion regarding those which exist preformed in it from the analyses of the ash of the salivary residue, as in the case of most of the other animal juices. We have, however, already remarked, that a great part of the *alkali* in the saliva is combined with ptyalin, from which it is separated by the weakest acids, as, for instance, carbonic acid. From the quantities of acids which are requisite for the saturation of alkaline saliva, Wright has concluded that in the normal state the alkali never amounts to 1% of the saliva. In the ash of the salivary residue the alkali is for the most part combined with *phosphoric acid;* thus Enderlin* found 28·122% of the tribasic, and Jacubowitsch 51·1% of the bibasic phosphate of soda in the ash

We never find more than a trace, and often not that, of the *alkaline sulphates* in fresh saliva; and even in the ash they are not found in any considerable quantity; hence, as in the case of the phosphoric acid, the sulphuric acid must have been formed from other compounds during incineration.

In the ash of human saliva Enderlin found 21·35% of sulphate of soda; and in that of horses' saliva I found 1·604% of this salt.

In Wright's method of determining the sulphocyanide of potassium, which consists in dissolving in water the extract taken up by ether, and precipitating with basic acetate of lead, not only sulphocyanide of lead, but a far larger quantity of a compound of lead with a fatty acid, is thrown down; from this circumstance Wright's determinations are on an average ten times too high.

The *chlorides of potassium and sodium* especially preponderate over the other mineral constituents of the saliva.

Enderlin found 61·930% of alkaline chlorides in the ash of the saliva, and Jacubowitsch 46·2%; in the dog they amounted, according to the last-named observer, to 85·7%.

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* Ann. d. Ch. und Pharm. Bd. 49, S. 317.

Sulphocyanide of potassium never occurs in the saliva except in very small quantity.

Jacubowitsch found 0·006% of this salt in his own saliva; and in analysing my saliva I found it to vary between 0·0046 and 0·0089%; according to Wright it ranges in human saliva from 0·51 to 0·98%, which is obviously far too high.

Although we have already spoken (in the first volume) of the existence of sulphocyanide of potassium in the saliva, yet the very dogmatical assertions of Strahl,[*] who denies that the presence of sulphocyanogen can be demonstrated, and applies to the experiments of his predecessors, such terms as "deficient, irregular, and ill-judged," (notwithstanding that Gmelin has exhibited pure sulphocyanogen in very large quantity from the saliva by distillation,) compel us to refer to the admirable memoirs of Jacubowitsch and Tilanus,[†] who have demonstrated beyond all doubt the presence of sulphocyanogen by the simplest and most unquestionable chemical experiments; Frerichs [‡] has also established the proof of the existence of sulphocyanide of potassium in the saliva. Moreover, it was formerly shown by Marchand,[§] and it has been more recently demonstrated by Wöhler and Frerichs,[||] by direct experiments, that sulphocyanide of potassium does not possess any poisonous properties.

Local stimulation of the salivary glands, the internal use of prussic acid and the salts of cyanogen, and especially of sulphur, increase, according to Wright, the quality of sulphocyanogen in the saliva.

In mixed or ordinary saliva the *ptyalin* is mixed with mucus, so that its properties do not appear to be altogether identical with those which we have described, and its accurate quantitative determination is impossible, independently of the considerable amount of salts contained in the aqueous extract. The aqueous extract, consisting chiefly of ptyalin, was found by Berzelius to amount to 40·8% of the solid residue of the saliva, while Gmelin fixed it at 20·0%, and Van Setten[¶] at 15·62%.

The determinations of the organic matter soluble in water and in alcohol, are very uncertain; indeed, little or nothing is known regarding this substance.

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[*] Med. Zeitg. v. d. Ver. f. Preussen. 1847. Nr. 21 u. 22.

[†] De Saliva et Muco; dissert. inaug. Amstelod. 1849.

[‡] Op. cit. p. 764.

[§] Lehrb. d. Phys. Ch. 1844, S. 410.

[||] Ann. d. Ch. u. Pharm. Bd. 65, S. 344.

[¶] Op. cit. p. 24.

The quantity of mucus in the mixed saliva must obviously be liable to very great variations, according to the conditions under which this fluid is collected.

The ether-extract ranged from 5·8 to 9·6% of the solid residue in the cases in which I determined it in several analyses of my own saliva.

In reference to the chemical *qualitative and quantitative analyses of the saliva*, it may be generally observed that the same principles and methods are applicable which have been described in the first volume, in our remarks on the different animal substances; hence we need here only refer to a few points which require a special mode of treatment. In the first place the saliva must always be filtered, in order to effect the removal of the epithelial scales; unfortunately, however, the saliva is often so viscid and tenacious, that it undergoes decomposition before passing through the filter; indeed, it generally happens that the small quantity of filtered and perfectly clear fluid begins to become turbid, while the greater portion of the fluid still remains upon the filter. In such cases it is often advisable to dilute the saliva with three or four times its volume of boiling water; and after the mixture has been as thoroughly as possible cooled, and the mucous flocculi for the most part deposited, to filter and proceed with the analysis; but as in this case we are not able to separate the soluble from the insoluble portion, it is better not to attempt the whole analysis, since we should only obtain inaccurate results. We might certainly at once evaporate the viscid fluid, in order to extract the residue with alcohol, ether, and finally with water; but independently of the circumstance that the aqueous extract is also difficult of filtration, substances would be taken up by the alcohol and ether, which do not pertain intrinsically to the saliva, but to the epithelial cells, and to the fat and remains of food sometimes mixed with them.

It is obvious that if, before submitting the saliva to a chemical analysis, we duly examine its morphological elements with the microscope, we can ascertain whether the insoluble parts of the saliva consist merely of epithelial cells and mucous corpuscles, or whether they also contain fat, vibriones, or molecular granules of an organic nature. In saliva which has been for a long time exposed to the air, in morbid saliva, and especially when it exhibits an acid reaction, such granules are of very frequent occurrence. As substances for the most part in an actual state of change, they do not fall within the domain of an accurate chemical analysis. No one can confound mineral substances, as, for instance, crystals of carbonate of lime, with these molecular granules.

If the saliva has been filtered, no interest attaches to any investigation of the residue left on the filter, at least in so far as the nature of the saliva is concerned, seeing that true saliva contains only soluble substances.

Wright finds his ptyalin in this residue; he cannot, however, possibly have treated this residue with sufficient water, since, in that case, it could not have contained so large a quantity of a matter soluble in water as his numbers indicate.

If carbonate of lime be mixed with this residue insoluble in water, it may easily be extracted by very dilute acetic acid, and its quantity subsequently determined.

In reference to the filtered solution, it is generally of interest to determine volumetrically the amount of acid which is saturated by a certain quantity of saliva, in order to form an opinion regarding the alkalinity of the saliva, or, in other words, regarding the quantity of the weakly-combined alkali. In every case, however, the filtered saliva must be neutralized with acetic acid, and then heated; if this gives rise to a turbidity, the albuminous substance which is precipitated must be collected on a filter, and determined quantitatively. The residue left on the evaporation of the filtered saliva is then to be treated in the same manner as we treat the residue in the case of most of the other animal fluids.

It only remains for us to make a few remarks on the quantitative determination of the sulphocyanogen. The following are at present regarded as the two best methods of effecting this object. One method consists in dissolving the alcoholic extract of the saliva in water, and filtering the fluid, which is generally turbid from the presence of fat; the filtrate, after being somewhat concentrated by evaporation, is heated with phosphoric acid, and distilled; the distillate is saturated with baryta, and the filtered fluid evaporated; the residue is then boiled for a long time with fuming nitric acid or aqua regia, and the quantity of sulphocyanide of potassium is calculated from the amount of sulphate of baryta which is separated. (Van Setten, Jacubowitsch, Tilanus.) In following the other method, we first precipitate the aqueous solution of the alcoholic extract with nitrate of silver, and treat the well-washed deposit with water containing nitric acid, which leaves the chloride of silver undissolved; we then precipitate the silver from the acid solution with hydrochloric acid, add a little chloride of barium, and evaporate slowly, adding from time to time some nitric acid: in this way also we obtain sulphate of baryta, from which the sulphocyanogen must be calculated. Before the addition of the baryta, we should also be able to precipitate the sub-sulphocyanide of copper by the addition of the sulphates of protoxide of iron and oxide of copper; as, however, the precipitate never consists of pure sub-sulphocyanide of copper, we are compelled to determine the sulphur as sulphate of baryta.

The application of basic acetate of lead, according to Wright's method, for the precipitation of the sulphocyanogen, is inapplicable in this case; for the sulphocyanide of lead is somewhat soluble in water, and the greater part of it would probably be lost on washing.

Abnormal constituents occur in the saliva probably more frequently than in many other animal secretions. It is very remarkable, that many mineral and organic substances which are thrown off by the urine either unchanged or little modified, are far more rapidly eliminated by the salivary glands—often, indeed, before they could be separated by the kidneys from the mass of the blood. We may very readily convince ourselves of this fact, by taking 5 grains of iodide of potassium in pills, when we shall find that it can be much sooner detected in the saliva than in the urine; in the latter fluid we may very often easily discover it after forty hours.

Moreover, when iodine is applied externally, as, for instance, in the form of ointment, it very rapidly passes into the saliva, where it may be recognized by nitric acid and a solution of starch, while it cannot be detected in the urine.

When iodine has been taken in the form of pills, and we have convinced ourselves, immediately after they have been swallowed, of the absence of this substance in the buccal mucus and in the saliva, we may very often detect it in the last-named fluid after a lapse of ten minutes, while it will not appear in the urine for a period varying from half-an-hour to two hours.

Bromine and *mercury*, and probably several other sialagogues, behave in this respect like *iodine*.

The reason why these substances so readily excite the flow of saliva, is probably solely dependant on the circumstance that they are separated from the blood by the salivary glands. It is possible that several organic sialagogues act simply in the same manner, namely, by some of their constituents, like the iodine, being readily separated by the salivary glands.

Wright and several other observers have been unable to detect any *mercury* in the saliva during mercurial salivation. I formerly had many opportunities of examining the saliva in cases in which salivation ensued during the treatment of syphilis by inunction practised by Rust and Louvrier, and I constantly found mercury in this fluid, both by dry distillation of the residue of the saliva, and by the simple application of an extremely small pair of plates of copper and zinc to the slightly acidified saliva. There are many reasons why, even when much mercury had been taken into the organism, none was found in the saliva; in the first place, it has very often been only buccal mucus which has been examined, for we may readily convince ourselves by the microscope, and more accurately by chemical analysis, that at the commencement of salivation scarcely any saliva is found in the sputa; the salivary glands are as yet not affected; the expectoration consists almost entirely of whole patches of epithelium and of mucus from the tonsils; and in products of this nature I have never been able to detect any mercury, even after its free administration; and, secondly, it has been forgotten by some experimentalists, that mercury volatilizes very readily with the vapour of water, so that, by evaporating too rapidly, and without sufficient care, they have allowed the little mercury that was present to escape.

Wright has injected alkaline carbonates into the veins of animals, and has found a consequent augmentation of the alkali in the saliva; when, on the other hand, he injected acetic acid or extremely diluted sulphuric acid into the vessels of healthy animals, he never found that an acid reaction of the saliva was induced.

It is singular that dogs into whose jugular veins Wright injected four ounces of pyroligneous acid, and half a drachm of sulphuric acid (although the acids were diluted with four and six ounces of water), bore this outrage so well, that after a short time they quite recovered,* and Wright found that their saliva had returned to its alkaline reaction. In cases in which I have performed similar experiments on animals, although for a different object, death was the invariable result—an event which may be very easily explained, since stasis must be very rapidly induced in the pulmonary capillaries, in consequence of the coagulation or gelatinising of the blood.

We have referred in the first volume to the incidental occurrence of *sugar* (p. 289) and of lactic acid (p. 94) in the saliva. It is extremely difficult to decide whether actual albumen coagulable by heat is present in a specimen of saliva.

Wright assumes that there are two different kinds of albuminous saliva, and as we have no experience on the point, we

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* [This is hardly correct. The dog into whose vein the pyroligneous acid was injected, died in about a week. See the "Lancet," 1842-3, vol. ii. p. 189.—G. E. D.]

cannot contradict his assertion; but as he also asserts that albumen occurs in normal saliva, which is certainly not the case, at least in any appreciable quantity, and as further, the recognition of small quantities of albumen is difficult and often impossible, for the reasons given in the first volume, we are justified in doubting whether albuminous saliva is of frequent occurrence.

Biliary matters, and especially cholesterin, sometimes pass, according to Wright, into the saliva. (See vol. i, p. 125.)

Wright has described a large number of varieties of saliva, classifying them according to the heterogeneous constituents which they contain; thus he distinguishes ammoniacal saliva, saliva containing hydrochloric acid, saline saliva, puriform saliva, bloody saliva, fetid saliva, &c. In declining to adopt Wright's results in our "Physiological Chemistry," we by no means wish to detract from the meritorious portion of his careful labours; but we do not think that the substrata on which such investigations are founded are of a nature to rank high in exact sciences such as chemistry and physiology. Descriptions of the subdivisions of morbid saliva, as for instance, of bilious, bloody, puriform, fetid, acrid, frothy, and gelatinous saliva, may have a certain importance in relation to semeiotics, but cannot serve as substrata for physiological inquiry. The illogical character of such a classification is obvious; the chemical investigations often do not justify the conclusions which Wright has drawn from them; for sugar, bile, lactic acid, &c., are never recognised by him with such certainty as chemists of the present day require; moreover, recent physiology might require further particulars regarding acrid, puriform, and bloody saliva, while our present pathology pays less attention to ontological ideas of disease than to investigations founded on actual physical diagnosis and on morbid anatomy. We repeat that we by no means wish to ignore the many interesting facts with which science has been enriched by Wright's rich experience and indefatigable labour.

Although *acid saliva* has been observed in a large number of instances, our knowledge of it is still very defective, for notwithstanding the positive assertions of Wright, there is as yet no proof that lactic acid is the cause of this acid reaction. Moreover, Prout* has adduced no decisive proof of the presence of this acid.

We have shown in the first volume, that the acid reaction of the animal fluids may depend on the presence of other acids (as for instance, several of the butyric acid group), or even of acid

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* On the Diseases of the Stomach, 4th ed. p. 451.

phosphate of soda: hence it is invariably necessary to determine the nature of the free acid, whenever it is present in the saliva, in different diseases, before we venture to decide regarding the course of the chemical process accompanying the disease; it is, however, the chief aim of all chemical investigations of animal objects, to draw from them a conclusion regarding the nature of the chemical process in the healthy or diseased state. For semeiotics the simple statement suffices that in this or that condition the saliva exhibits an acid reaction. We shall now briefly mention those pathological states in which, as yet, the saliva has been found to present an acid reaction.

The saliva is *acid*, according to Donné,* in inflammatory affections of the *primæ viæ*, in pleuritis, encephalitis, acute rheumatism, intermittent fever, and uterine affections, and, according to L'Héritier, also in cancer of the stomach. Wright assumes that there are four varieties of acid saliva, namely, (*a*) that which occurs in idiopathic affections of the salivary glands; (*b*) that which presents itself when there is a predominance of acid in the organism generally, from constitutional or other causes, amongst which he mentions scrofula, phthisis, rachitis, amenorrhœa, inflammatory rheumatism, &c.; (*c*) the form occurring in sub-acute inflammation of the mucous membrane of the stomach and intestines; and (*d*) the form presenting itself in dyspepsia (a somewhat vague mode of expression). In affections of the nervous system, the saliva is on the other hand never acid, but often very strongly alkaline. In catarrhal affections of the gastric and intestinal mucous membranes and in the round perforating form of ulceration of the stomach, I have very often, but not invariably, found the saliva acid; in cancer of the stomach and in diabetes, I have, however, always found it acid. In inflammatory affections of the thoracic organs, in acute rheumatism, typhus, &c., I † have very often found the saliva alkaline or perfectly neutral. According to Donné and Frerichs‡ the acid reaction always depends on the buccal mucous membrane, which, when in a state of abnormal irritation, invariably yields an acid secretion.

Amongst the difficulties which usually present themselves in the investigation of morbid saliva, we may notice that we can rarely obtain a quantity sufficient for analysis, seeing that it is a fluid which contains only a very small amount of solid constituents.

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* Histoire physiol. et pathol. de la Salive. Paris, 1836.

† Schmidt's Jahrb. Bd. 36, S. 185.

‡ Op. cit. p. 761.

Hence it might be expected that it would, at all events, have been more accurately examined in persons with ptyalism, in which it is secreted in large quantities, but such is not the case. Wright has indeed given an exposition of those cases in which a symptomatic, a critical, or an artificially induced ptyalism occurs; but we do not the less miss analyses susceptible of chemical and physiological application. The secretion in cases of *mercurial salivation* has as yet been the most carefully studied. The results obtained by Wright, L'Héritier, Simon, and myself, perfectly coincide in the following points. At the commencement of mercurial salivation the buccal mucous membrane and the tonsils are more affected than the salivary glands, and hence the expectoration is more viscid, of a higher specific gravity, and richer in solid constituents, especially epithelium and mucus-corpuscles, than normal saliva; it is very turbid, from the presence of more or less distinct flocculi; has an alkaline reaction; contains little of the peculiar principle, ptyalin, often much fat, and rarely any appreciable quantity of sulphocyanide of potassium. At a later period, when the salivary glands become the seat of pain and swelling, a less turbid saliva is secreted, which often contains a much smaller amount of solid constituents than normal saliva; it is still alkaline, and sulphocyanide of potassium is more often absent than present; it is also rich in fat, and often in mucus-corpuscles. We have already noticed the presence of mercury in this variety of saliva.

In conclusion, we must mention *salivary calculi* as morbid products of this secretion: they have been very often analysed, and have been found to contain more carbonate of lime than any other kind of concretion. As we have already shown that the saliva even of carnivorous animals holds in solution no inconsiderable quantity of lime in combination with organic matter, and that the lime is very readily separated from this compound as a carbonate, we have no difficulty in comprehending the mode of formation and the constitution of these concretions.

The quantity of saliva excreted in a given time is a point regarding which there is a tolerable coincidence amongst the statements of authors, although we cannot regard it as definitively established; for most writers have based their calculations on the data of Mitscherlich, which refer merely to the parotid secretion of a man labouring under disease.* The patient in the case referred to, after collecting the saliva in the mouth for 15 minutes, ejected from it

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* [Lehmann should have mentioned that in this case the patient had a parotid fistula.—G. E. D.]

6·27 grammes, while during the same period 0·92 of a gramme were discharged by the fistula; moreover Mitscherlich never determined the quantity of the parotid secretion, except under definite relations and in given times. Now if we assume that the above ratio of the parotid secretion to the secretion of the other salivary organs is constant, which, however, is more than doubtful, we may calculate the quantity of saliva which will be secreted in a definite time, or under definite physiological relations. Under ordinary circumstances (that is to say, on the common hospital diet) Mitscherlich found that the quantity of the parotid saliva in 24 hours varied from 46·3 to 74·8 grammes. Assuming the above ratio of the parotid secretion to that of the other sources of the saliva to be constant, the whole amount of saliva from the six salivary glands and the buccal mucous membrane, would amount on an average to 473 grammes in 24 hours. Burdach* calculates, from Mitscherlich's data, that the saliva secreted by an adult in 24 hours amounts to 10 (German) ounces (= 255 grammes). Valentin† assumes the quantity at from 216·4 to 316·3 grammes; Donné‡ fixes the quantity at 390 grammes, and Thomson§ at only [3216 grains or] 210 grammes.

Jacubowitsch has determined in dogs the quantities of saliva which he could collect from each set of salivary glands in an hour; from the two parotids he obtained 49·2 grammes, from the submaxillary glands 38·83 grammes, and from the orbital and sublingual glands, and the buccal mucous membrane, 24·84 grammes. We can draw no conclusions from these data, regarding the quantity of saliva secreted in a normal state in a definite time; for, independently of the circumstance that nothing is stated regarding the size or the weight of the dog, we know from his numerical statements, that Jacubowitsch employed dogs of various sizes in his experiments, so that the fluid was collected under such peculiar conditions, that a comparison of it with the quantity of the secretion in the normal state is impossible. Jacubowitsch, however, arrived at the interesting result, that to whatever extent the quantities of the saliva secreted by the different organs may vary, the solid constituents—both the organic and the inorganic substances—amount to very nearly the same from all three of the sources; thus, in the quantities above given of parotid, sub-

* Physiol. Bd. 1, S. 277 ff.

† Physiol. d. Menschen. 1844. Bd. 1, S. 626.

‡ L'Institut, No. 158, p. 59.

§ Animal Chemistry. Lond. 1843, p. 571.

maxillary, and sublingual saliva, the solid constituents amount to very nearly the same, that is to say, to about 0·232 of a gramme, of which 0·080 is organic and 0·152 inorganic matter.

All determinations of the quantity of saliva secreted during a more prolonged interval (as, for instance, 24 hours), must at most be regarded as merely approximative, since the activity of the salivary organs is dependent on very different influences and conditions. The most common cause exciting a copious discharge of saliva is the mastication of food; it depends, however, very much on the nature of the food, whether much or little saliva is effused into the buccal cavity; dry and hard food inducing a more copious flow of saliva than food which is moist and soft; indeed, the mere motion of the lower jaw excites the act of secretion, and hence, speaking or singing is always accompanied by the secretion of saliva. That chemical irritants, such as are present in acid and aromatic articles of food, and mechanical irritation, such as tickling the palate, often produce an immediate secretion, is as well known as that certain psychical influences always produce a similar effect. It is especially important to observe that after the use of food, the secretion continues for a long time; a phenomenon which appears not to be so referable to the irritation transmitted to the salivary glands from the buccal cavity, as to the communication of nervous action from the stomach during the process of digestion; for, on introducing food into the stomach, either through a gastric fistula, or by means of an elastic tube in the œsophagus, we observe that the secretion of gastric juice is accompanied by a copious effusion of saliva.

In order to determine the quantity of saliva required for different kinds of food, experiments have been instituted by Magendie and Rayer,* by Lassaigne,† and by Bernard,‡ on horses. The œsophagus was exposed and opened, and the food which the animals had swallowed was intercepted and removed. From these experiments it followed, that straw and hay, as they pass down the œsophagus, are mixed with four or five times their weight of saliva, whilst seeds abounding in starch, as, for instance, oats, are mixed with an equal quantity, or perhaps one and a half times as much of saliva, and fresh green fodder with only half its weight; and that food mixed with water seems to take up scarcely any saliva. Hence it appears as if, when food is taken, the secre-

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* Compt. rend. T. 21, p. 902.

† Journ. de Chim. Méd. 1845, p. 472.

‡ Arch. gén. de Méd. 4 Sér. T. 13, p. 22.

tion of saliva is only dependent on its nature, and as if, when fluid or moist food is taken, the glands are not excited to activity. We must, however, assume with Frerichs, that even in a state of perfect repose, the secretion of saliva is not totally suspended; for although Mitscherlich found scarcely a trace of saliva escaping from the fistulous openings in the patients on whom he experimented, when they had fasted for some time and were in a state of perfect repose, and although we observe scarcely any secretion in horses in whom a fistulous opening has been established, when they have not been supplied with food for some time, we cannot suppose that the process of secretion is absolutely suspended in these any more than in other glands. Moreover we can form no opinion regarding the normal secretion in a state of relative repose, from the facts that during sleep, when the head is inclined forwards, and in paralysis of the facial muscles, saliva is secreted in no sparing quantity, since in both those cases the abundance of the secretion is dependent on peculiar conditions.

Physiologists have ever held the most varied opinions regarding the *physiological value* of the saliva. We must, however, regard the saliva as essentially fulfilling a threefold object of a mechanical, a chemical, and a dynamical nature.

The *mechanical* object is so manifest, that no one has ever seriously doubted it; for it is obvious to our senses, and requires no demonstration to convince us that the moistening of dry food in mastication serves, on the one hand, the better to adapt it for deglutition, and, on the other hand, to separate the particles, and thus allow them the more freely to be acted on by the other digestive fluids. Formerly, however, the whole value of the saliva was limited to this function; and Bernard recently believed that he had proved this view to be correct by the experiments to which we have alluded. He maintained that the parotid saliva, by its thin fluid property, serves to moisten the food, while the tough and viscid secretion of the submaxillary glands affords a mucous investment to the masticated food, lubricates it, and thus adapts it for deglutition.

We have already seen that the secretion of the submaxillary glands is distinguished by its viscidity and toughness from the parotid secretion, and even that infusions of these glands differ in the same manner. In reference to this circumstance Bernard notices the fact in comparative anatomy, that those animals which swallow their food without masticating it, as, for instance, serpents, birds, and reptiles, possess no parotid glands, or at most only rudimentary organs, while their submaxillary glands for the elaboration of mucus are for the most part very well developed.

The *chemical function* of the saliva is a subject on which different observers have held very different views. Leuchs was the first who was led by experimental inquiry to the discovery that starch is gradually converted into sugar by the action of the saliva. Subsequent inquirers who have repeated the experiments in some instances confirm, and in others deny, the accuracy of his views. Wright, who bases his view on a large number of experiments, speaks very decisively in favour of the chemical action of saliva on amylaceous food; and indeed, Mialhe* believed that he had actually discovered the substance in which this metamorphic power solely or for the most part resides, and gave it the name of *salivary diastase.* Several observers, having failed in attempting to confirm the views of Wright and Mialhe, have directed their attention to the individual secretions of the different glands. Magendie was the first who discovered that neither the parotid nor the submaxillary secretion exerts any action on starch, but that the common or mixed saliva of the horse converts both crude and boiled starch into sugar at the temperature of the animal body; Bernard attributed this unquestionable property of the mixed saliva (whether obtained from man, the dog, or the horse), solely to the buccal secretion, while Jacubowitsch has adduced convincing evidence that this secretion alone does not possess the above property which exists only in the mixture (whether artificial or natural) of the secretions of the buccal mucous membrane and the salivary glands. It can therefore no longer be doubted that the saliva, in the normal condition in which it is mixed with the food, possesses the property of converting starch into sugar. We by no means, however, agree with Ross† in regarding the buccal cavity as the stomach for vegetable food. Even under the most favourable circumstances we cannot detect a trace of sugar in a mixture of saliva and boiled starch, in less than from 5 to 10 minutes; and hence, if the conversion of amylaceous matter into sugar be the physiological function of the saliva, its action must not be confined to the short time in which the food remains in the mouth, but must also be continued in the stomach and intestines. Now we may readily convince ourselves that this is really the case, by observing what occurs in an animal in whom a gastric fistula has been established; for while pure gastric juice

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* Compt. rend. T. 20, pp. 247, 367, 954, et 1485.

† The Lancet, January 13, 1844.

exerts no action on starch, sugar may be detected by the ordinary means in the stomach of the animal in 10 or 15 minutes after it has swallowed balls of starch, or after they have been introduced through the fistula. Hence it cannot be doubted that the saliva, after it has been mixed with the other animal secretions, continues to exert its action on the *amylacea* in the digestive canal.

Notwithstanding the evidence which has been adduced to prove that the saliva exerts this action on starch, there are other facts which seem to show that we must not assign to it an extreme importance in the digestive process in general. For, even if we do not admit the conclusiveness of Budge's* experiment, in which he extirpated all the salivary glands of a rabbit, and afterwards observed no disturbance of the digestive system, and no imperfection in the nutrition, yet on the following grounds we must regard this action of the saliva as a somewhat limited one: the quantity of the saliva which is secreted is altogether independent of the quantity of starch contained in the food, and is extremely small when the latter is taken in a fluid form; when food which has been thoroughly moistened is swallowed, there is only a very slight secretion of saliva; liquid and moistened foods remain in the stomach so short a time, that a perfect conversion of the starch into sugar in this organ is impossible; nature has, however, provided a secretion which is poured into the duodenum—the pancreatic juice, which possesses the power of effecting this conversion of starch into sugar in a far higher degree than the saliva; animals (fishes, for instance) which swallow amylaceous food without masticating it, possess for the most part such rudimentary salivary glands, that the secretion from them can hardly be taken into consideration. But even the pancreatic juice is not generally sufficient to effect the perfect metamorphosis of the starch; the conversion proceeds so slowly that we can almost always detect a considerable quantity of starch in the excrements not only of carnivorous but also of herbivorous animals, after the ingestion of amylaceous food. Hence it appears very much to depend on the subjective opinions of different writers, whether a greater or lesser importance in this point of view be attributed to the saliva; in no case, however, should the function of the saliva as a saccharifying agent be overrated.

This is a subject on which special observations, experiments, and criticism, are peculiarly needed; and it is by the neglect of this mode of inquiry that some of the best observers have been

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* Rhein. Blätt. Bd. 4, S. 15.

erroneously led to adopt the most extreme views. The difficulty of forming a decided judgment without a special investigation will be best seen from the following historical sketch of the facts which have been accumulated in reference to this subject. Wright,[*] whose views are based on a large number of experiments, is one of the strongest supporters of the digestive powers of the saliva; and I[†] formerly entirely coincided in this view; but all experiments and results bearing on this point must only be adopted with the greatest caution, for there is no analytical inquiry in which, under apparently precisely similar relations, the same experiment so often yields different results, and in which quantitative determinations so invariably present a want of uniformity. Thus, the quantities of starch converted into sugar in contemporaneous experiments with the same saliva, and at perfectly equal temperatures, are often extremely different. Even when there is only a very small quantity of starch in relation to the saliva, we almost always find that the whole of it has not undergone conversion into sugar, as was observed by Jacubowitsch; it is only after a very considerable time, seldom before from 16 to 24 hours have elapsed, that we find the whole of the starch changed; and then the starch is not merely converted into sugar, but this latter substance has already undergone further changes, and has given rise to the formation of lactic acid—a change which often commences while very large quantities of starch still remain unchanged. We must further bear in mind that many other animal substances under certain conditions possess a similar power of converting starch into sugar. Liebig long ago observed that gelatin and albuminous and gelatigenous tissues, when they had been lying in a state of moisture, and exposed for some time to the atmosphere, possessed the property of effecting this change. Magendie[‡] subsequently convinced himself that infusions of cerebral tissue, of heart, liver, lungs, and spleen, possessed to a certain degree the power of converting starch into dextrin and sugar; he likewise found that the serum of blood at 40° possessed this property, and that boiled starch was converted into sugar even in the circulating blood of the living animal. Hence Bernard[§] merely repeated the experiments of Liebig and Magendie, when he exposed well-prepared and cleaned buccal mucous membrane to the air, and subsequently

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[*] Op. cit.

[†] Schmidt's Jahrbb. Bd. 37, S. 121-123, Bd. 39, S. 155 ff.

[‡] Compt. rend. T. 23, pp. 189-192.

[§] Arch. gén. de Méd. 4 Sér. T. 13, p. 10.

observed its action on starch. These facts cannot, however, be placed in comparison with the action of the mixed saliva, which does not require any long exposure to the atmosphere in order to acquire this property, and is only exceeded in this power by the diastase of germinating seeds and by the pancreatic juice.

Another point which must appear doubtful to those who have not experimented for themselves, is the question whether acid saliva has the same saccharifying force as the alkaline secretion—a view most positively denied by Sebastian, Wright, and Bernard; and as confidently asserted by Jacubowitsch and Frerichs. In my former experiments I failed, like the first-named observers, in effecting the conversion of starch by saliva, and notwithstanding the most careful inquiry, I have been unable to detect the causes of that failure; but in my more recent experiments, when I have allowed saliva treated with acetic, sulphuric, hydrochloric, or nitric acid, to act on either crude or boiled starch, I have always observed a tolerably rapid formation of sugar, and have convinced myself that acids can no more impede the digestive power of the saliva than alkalies can promote it. It is therefore certain that mixed saliva, whether it be alkaline or acid, acts on starch with equal energy at equal temperatures. Trommer's sugar-test cannot be directly applied in this investigation, for Frerichs has shown by an interesting experiment that suboxide of copper is immediately separated when saliva and starch are boiled with potash and sulphate of copper; we must, therefore, remove any starch or dextrin that may remain in the filtered fluid, by treating it with alcohol, before applying Trommer's test, or we must adopt some other means of demonstrating the presence of sugar in the mixture.

The albuminous substance occurring in the saliva, to which Mialhe has given the name of *Diastase salivaire,* is undoubtedly similar in many respects to diastase; but, on a rigid examination, the two substances are found to be altogether different. Mialhe obtains this salivary diastase by precipitating human saliva with absolute alcohol. On referring to the composition of saliva, it is easy to perceive that the substances which will be precipitated by alcohol are chiefly ptyalin and mucus with a quantity of salts, and it is in the mixture of these substances that Mialhe thinks that he has found the active principle of the saliva. In experiments with this mixture, I have altogether failed in obtaining evidence of the extraordinary powers which were attributed to it by Mialhe (who maintains that 1 part can rapidly effect the metamorphosis of 8000 parts of starch at a temperature of 37°); and although I formerly believed that I had obtained a somewhat similar result, I have since convinced myself that the metamorphosing force is neither concentrated in the admixture of substances indicated by Mialhe or by myself, nor yet in any other part of the extractive matters of the saliva. In the mean time, it would be unscientific to neglect all inquiry regarding this peculiarity of the saliva, or rather of one of its constituents, and to rest satisfied with the fiction that all exciters of fermentation are substances undergoing changes, and that such substances are incapable of being submitted to chemical exhibition and investigation. All fictions that close the door on inquiry are to be rejected, unless they admit of a logical justification. If Schwann, Wasmann, and others, had remained satisfied with the conviction that the cause of the digestive power of the gastric juice did not admit of being investigated, we should not have advanced very far in the knowledge of the process of digestion. We can hardly condemn an inquiry into the hypothetical diastase of the saliva as absurd; for the saliva does not lose this property either by the action of heat or alcohol, and pepsin similarly retains its power even after having previously been combined with salts of lead. This much, however, is certain, that the ptyalin obtained by Berzelius, Gmelin, and Wright, was found in all cases to be deficient in the power of converting starch into sugar.

After it had been demonstrated, as already observed, first by Magendie, and subsequently by Bernard, that the secretions of some of the salivary glands did not exert any metamorphic action on starch, Jacubowitsch, under the direction of Bidder and Schmidt, prosecuted some admirable experiments on this subject, which we do not think it will be irrelevant to notice at some length in the present place. He convinced himself, by hindering the flow of the secretions of the parotid and submaxillary glands from entering into the mouth of a dog, that the mere secretion of the mucous membrane of the mouth (contrary to Bernard's assertion) was unable to convert starch into sugar. But when he tied the ducts of only a single pair of glands (excluding only the secretion from the parotid or that from the submaxillary glands), and suffered the dog to recover after the operation, and then, according to Bernard's method, as already described, digested starch with the saliva exuding from the open and depressed mouth of the dog, some of the starch was converted into sugar in the course of five minutes. The starch was also quickly metamorphosed when brought in contact with an artificial admixture of the above-mentioned glandular secretions and buccal or even nasal mucus. (The nasal mucus alone did not possess this property). A mixture of the secretions of the parotid and submaxillary glands, without any secretion from the mucous membrane, was entirely deficient in this property.

To prove that the action of the saliva on starch is continued in the stomach, the same author instituted the following experiments: in one case he fed a dog in whom a gastric fistula had been established, upon boiled starch after a twelve hours' fast; repeated experiments showed that the contents of the stomach which were discharged from the fistula contained sugar. In another case Jacubowitsch introduced boiled starch through a fistulous opening into the stomach of a dog, in whom the excretory ducts of the salivary glands had been tied; but here he could not discover any trace of sugar in the contents of the stomach after a prolonged period.

Wright attaches a very high degree of importance to the alkalinity of the saliva both during insalivation and during gastric digestion, and ascribes to it a second chemical function, viz., that of saturating the excessive quantity of acid introduced into the stomach or formed within it. It is certainly an undeniable fact that alkaline saliva is secreted after the ingestion of acid food; but this also occurs when highly seasoned food, spirituous liquors, and other stimulants have been taken, which cannot have been saturated or combined, like the acids, with the alkali of the saliva. It is extremely doubtful whether the object of this secretion is to saturate the free acid, since our experiments have in general rather tended to show that an excess of acid in the stomach is less injurious to the digestion of nitrogenous substances than any deficiency in its quantity. For the present, therefore, we must rest satisfied with admitting that as the saliva constantly becomes alkaline during or after eating, even in those cases in which it was acid before the ingestion of food, and as moreover its alkalinity increases after taking indigestible or acrid substances, the alkali probably contributes to promote the function of the saliva, although we must leave it to future enquirers to determine the manner in which this object is effected.

Wright supports his assertion by an appeal to his own experience; he found that the effect of spitting, after having partaken of a full meal, was alway to induce an abundance of acidity with much pain in the stomach, and a corresponding alkalinity in the saliva.

The saliva exerts no metamorphic action on any of the carbohydrates excepting starch: cane-sugar, gum, vegetable mucus (bassorin), and cellulose, remain unchanged in the saliva; it is only in certain species of sugar, and after long-continued digestion at a high temperature, that we observe the formation of lactic and subsequently of butyric acid.

The saliva exerts no action whatever on albuminous and gelatigenous food; its utmost effect being to relax their tissues like pure water, and thus to render them more accessible to the action of the gastric juice.

Wright thought he had convinced himself from numerous experiments that flesh is softened and rendered tender in its texture much more rapidly when digested with saliva, than when it is subjected to the action of water; he further concluded from these and similar experiments, that the saliva contributes essentially to the digestion of animal substances; but Jacubowitsch and Frerichs have recently shown by their more accurate and well-tested experiments, that this view is utterly erroneous.

Bernard and Barreswil* believed that they were justified from some of their experiments in laying down the following proposition: "Le suc gastrique, le fluide pancreatique, et la salive, renferment un même principe organique, actif dans la digestion: mais c'est seulement la nature de la réaction chimique, qui fait differer le rôle physiologique de chacun de ces liquides, et qui determine leur aptitude digestive pour tel ou tel principe alimentaire."

If this view had not been fully controverted by the admirable experiments of Jacubowitsch and Frerichs, its untenability would have been manifest to every one on a mere repetition of Bernard and Barreswil's experiments.

Liebig has suggested that the saliva may be designed, from its tendency to frothing, to convey atmospheric air into the stomach and intestinal canal. Wright and others subsequently to him have shown that starch is metamorphosed by saliva obtained by expectoration, (which has consequently been sufficiently exposed to the action of the air,) without further access of oxygen; and Valentin† has very correctly stated that oxygen is not necessary for the digestion of animal substances by the gastric juice—facts which have been advanced in refutation of Liebig's view; but it should be borne in mind that these experiments were not conducted with such accuracy as to exclude all access of oxygen, and that they cannot therefore be advanced as sufficient evidence

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* Compt. rend. T. 21, p. 88.

† Lehrb. d. Physiol. des Menschen. Bd. 1, S. 286.

against the accuracy of Liebig's view: there are, moreover, as we know, certain processes, as for instance the vinous fermentation, in which it requires the greatest exactitude of observation to demonstrate the necessity of a slight access of oxygen. Then again, the fact that only mixed saliva, that is to say, saliva which has been in contact with atmospheric air, is capable of metamorphosing starch, speaks rather in favour of Liebig's view than against it. Even if the oxygen, which undoubtedly passes into the *primæ viæ* with the saliva, exerts no effect upon the process of digestion in the stomach, the use of this gas in the intestinal canal may readily be understood, although it cannot be specially demonstrated. We know that gases are present in the intestinal canal, and that these gases are rich in carbonic acid and often also in hydrogen compounds. The formation of the latter, whose passage into the blood would be followed by very injurious results, must necesssarily be greatly limited by the presence of free oxygen. According to the laws of the diffusion of gases, the presence of oxygen in the intestines must diminish the withdrawal of oxygen from the blood and the supply of carbonic acid and hydrogen to that fluid.

Wright considers that one of the most prominent functions of the saliva is its supposed property of serving as a necessary *stimulant to the stomach*, and thus promoting the digestive process. We have already frequently expressed our dissent from the *dynamical* explanation of physiological phenomena; according to our view, even the nerves cannot act independently of chemical changes, and if we are to admit the control of dynamical forces on the nervous system, we must first establish the existence of definite chemical relations in proof of such an action. It appears to us altogether inconsistent to attach any importance in physiological chemistry to the obscure idea of an *irritant*. When I introduced fresh saliva, through a fistulous opening, into the stomach of a dog, I observed that the same amount of gastric juice was secreted as when other mucous fluids were conveyed into the stomach. There is no indication of any special irritant in experiments of this kind; and the stimulating action of the saliva can hardly be required for the process of gastric digestion, since solid substances, and more especially nitrogenous food, induce a far more abundant secretion of gastric juice than pure saliva.

Wright introduced from 3 to 10 ounces of saliva, through an elastic-gum catheter, into the stomachs of dogs that had been kept fasting, and observed, after the lapse of ten minutes, contraction of the abdominal muscles, uneasiness, eructations, and vomiting.

I did not perceive any of these phenomena when I introduced fresh human saliva into the stomach of a dog, through a fistulous opening, but I certainly did not employ more than two ounces at most; six ounces of the parotid saliva of a horse were, however, equally well retained by the dog. Nor can any conclusions be deduced from vomiting in dogs, since they vomit on the slightest provocation, and frequently devour what they have thrown up without experiencing any bad effect from it. The quantity of saliva which was used by Wright, and which could not have been very speedily collected, leads us to suspect that his "normal saliva" was already undergoing decomposition, and consequently gave rise to these abnormal phenomena.

Wright also distinguishes several passive functions of the saliva; (*a*) it assists the sense of taste; (*b*) it favours the expression of the voice; (*c*) it clears the mucous membrane of the mouth, and moderates thirst.

We must not omit to mention, at the close of these remarks on the saliva, that Wright believes he has confirmed, by his experiments of injecting the saliva of animals into the blood, the ancient opinion, which, however, is still maintained by Eberle* and Hünefeld,† that the saliva of enraged animals, or of men in a violent fit of anger, is capable of inducing a number of highly suspicious, morbid symptoms, and more especially hydrophobia, when introduced into the blood. In the experiments made by Prinz and myself on dogs, with human saliva and the saliva of a horse, and conducted very nearly in the same manner as Wright's, excepting that we employed only filtered saliva, we never observed any symptoms of hydrophobia, even in dogs that suffered from the experiment, nor did we recognize, in the dissection of these animals, any of the pathologico-anatomical phenomena (as, for instance, in the stomach) which are usually met with in the *post mortem* examination of mad dogs. Jacubowitsch‡ has also devoted the most careful attention to this subject, and instituted very accurate experiments, which not only refute Wright's statements, but expose at the same time the grounds that had led to the erroneous views arising from these experiments. The results of Jacubowitsch's experiments are as follows: human saliva does not give rise to any morbid symptoms, even when introduced in large quantities into the stomachs of dogs: unfiltered saliva pro-

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* Physiol. der Verdauung. Würzburg, 1834, S. 28.

† Chemie u. Medicin. S. 52.

‡ Op. cit. pp. 42-47.

duces symptoms of choking when injected into the veins: filtered saliva (which has been freed from epithelium, and other morphological substances which might obstruct the capillaries of the lesser circulation) may be injected with perfect impunity. The saliva collected during smoking contains empyreumatic substances, which give rise to symptoms of narcosis when the fluid is injected into the stomach or veins. Hertwig* has shown, by numerous experiments, that even the saliva of mad dogs, when inserted into the stomachs of other animals, or when they are inoculated with it, is unable to produce hydrophobia.

GASTRIC JUICE.

The fluid which accumulates in the stomach after the ingestion of food, is in its pure state perfectly clear and transparent, almost entirely devoid of colour, having at most but a very faint yellow tint; it has a very faint, peculiar odour, and a scarcely perceptible saline-acid taste, and is a little heavier than water; only a few morphological elements can be perceived in it; and these consist partly of unchanged cells of the gastric glands, partly of the nuclei of these cells, and partly of fine molecular matter, which is produced by the disintegration of these elements. Its reaction is very acid; it is not rendered turbid by boiling; when neutralized with alkalies a slight turbidity may sometimes be remarked. The gastric juice is distinguished from most other animal fluids by the circumstance that it remains for a very long time undecomposed, and that even when a fungous growth (mould) has appeared, it always still retains its most essential character, namely, its digestive power.

The best method of obtaining gastric juice in a state of the greatest possible purity, is to feed dogs, in whom gastric fistulæ have been artificially formed, with bones which they can readily break to pieces; in the course of from 5 to 10 minutes to open the outer closed extremity of the fistula; and by means of a funnel and catheter to collect the escaping juice, and to separate it by filtration from flocculi of mucus, and any fragments of food that may be present. It is, however, an objection that a considerable

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* Beiträge zur nähern Kenntniss der Wuthkrankheit. Berlin, 1829, S. 156.

quantity of saliva is always mixed with gastric juice obtained in this manner.

Formerly the only method of obtaining gastric juice in any available quantity was to feed animals which had been for a long time kept fasting, and to kill them in from 10 to 30 minutes afterwards. If we employ bones, tendons, or large pieces of flesh, we generally find in the stomach of the animal a gastric juice which is very suitable for the purpose of experiment, since it possesses all the properties of a normal gastric juice obtained in the preceding manner; if, however, the animals have been for a long time fasting, rather more mucus is present; this is the only difference I have ever observed. Tiedemann and Gmelin used no gastric juice in their investigations which was not collected in this manner; but in place of the above-named food they used irritant and insoluble substances (pepper-corns and pebbles).

It must be observed that this method answers very well with carnivora and omnivora, but not with herbivora (unless with ruminants); for in the latter, at all events, in rabbits, we often find that after very prolonged fasting (even after the animal has died from inanition), the stomach is still full of the remains of food; in this manner, however, we never obtain a pure gastric juice, but one always containing saliva. Moreover, it is obvious that it is not a very satisfactory or useful method, since we never obtain from it more than a small quantity of gastric juice, and a large number of animals must be killed in order to obtain a sufficient quantity for the purpose of analysis or experiment.

Spallanzani, Braconnot, and Leuret and Lassaigne, obtained gastric juice without killing the animals, by making them swallow sponges attached to a string, and after some time withdrawing them from the stomach. Although these experimentalists, with the aid of this method, made many beautiful observations, and threw much light on the mysterious digestive fluid, the objections pertaining to this means are so obvious as not to require mention; the greatest being that in this way we not only collect an impure gastric juice, but that the quantity which we obtain is also very small.

The third and best method is that which we first mentioned, depending on the establishment of artificial gastric fistulæ. After Beaumont's* most admirable and decisive observations on gastric digestion, which were instituted on a man in whom a gastric fistula had become formed, in consequence of a gun-shot wound,

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* Experiments and Observations on the Gastric Juice, and the Physiology of Digestion. Boston, 1834.

we are in the next place indebted to Blondlot* for producing such fistulous openings in dogs. I have not found the establishment of these fistulæ by any means so easy a matter as would be inferred from Blondlot's description. A number of causes may intervene to prevent the operation from terminating favourably. Foremost amongst these, I may mention that the dogs generally bite away the ligature and the plug to which the thread passing through the stomach is fastened, and pull out the thread, so that a rupture of the stomach ensues, which is perfectly certain to cause the death of the animal; and the application of a starch bandage is seldom of any use in preventing this mischief, unless the animal be so securely tied that he cannot move himself. This cruel procedure must, further, be continued for some time, since the subsequent application of sponge plugs to dilate the fistula requires equal precautions. Hence, as far as my own experience goes, I can only recommend Bardeleben's† method of establishing such fistulæ, by which the above and many other objections to Blondlot's procedure are avoided.

According to Bardeleben, the following is the best method of proceeding. We make an incision two inches in length from the ensiform process towards the umbilicus, exactly in the linea alba; after perfectly separating the abdominal walls, we open the peritoneum for an equal length, and with two fingers seize the stomach (which, if the animal has been fed shortly before the operation, is very easily accomplished); we then form a fold about an inch in length, (in which we must take care that no large blood-vessels are running), pass a ligature through it with a strong needle, and fasten the fold to a wooden peg placed transversely across the wound, which must be closed by stitches passing of course through the abdominal walls; the fold of stomach must then be included in the angle of the wound lying nearest to the navel, in order that the thread shall not cut the fold in the violent movements which accompany the vomiting that often ensues, and in which the stomach is forcibly drawn inwards. Bardeleben lays it down as a very important rule, that a doubled thread should be drawn through the abdominal muscles and fold of stomach, and that the two ends of one thread should be tied in front of the portion of stomach thus artificially prolapsed, and those of the other behind it. The wound then requires no further treatment (and this in

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* Traité analytique de la Digestion, considérée particulièrement dans l'homm et dans les animaux vertebrés. Nancy et Paris, 1843.

† Arch. f. phys. Heilk. Bd. 8, S. 1-7.

Blondlot's method is a matter of very great difficulty); the animal's licking does no harm, since it only keeps the wound clean. The included portion of stomach soon becomes gangrenous (generally from the third to the fifth day), and is then thrown off; the fistula is then completed. To introduce a suitable canula into the fistula, which shall neither fall out nor press too hard, nor when closed shall allow fluid to escape from the stomach, is a matter of much greater difficulty. For this purpose Bardeleben has also contrived a very simple and useful apparatus, namely, a silver tube, about three-fourths of an inch long, provided at one end with a projecting border, in place of the double button-like instrument used by Blondlot: into this tube there are fitted two double hooks, united by a wire of the same length as the canula; by a well-fitting cork these hooks are so pressed upon the walls of the canula, as to render it impossible for the whole apparatus to escape from the wound. For further particulars regarding details of manipulation, I must refer to Bardeleben's memoir.

Pure filtered gastric juice contains only a small amount of solid constituents, namely, from 1·05 to 1·48%; and hence they, and especially the organic ingredients, have been very little examined.

In a specimen of human gastric juice collected by Beaumont, Berzelius found 1·27% of solid constituents; in the gastric juice of a dog, Blondlot found 1·00, and Leuret and Lassaigne 1·32%; and in that of a horse, Frerichs found 1·72%. I have derived the above-named numbers from experiments on the gastric juice of various dogs; it must, however, be remarked than on evaporation, the gastric juice not only loses water, but also a comparatively large quantity of hydrochloric acid, as will be seen from the experiments presently to be described. Hence it was that Tiedemann and Gmelin found that the solid constituents amounted to 1·95% in the gastric juice of a dog to whom carbonate of lime had previously been administered, the hydrochloric acid being thus prevented from escaping, and chloride of calcium being formed.

Very different opinions have been held, up to the most recent times, regarding the nature of the free acid of the gastric juice. Prout was the first who instituted any serviceable chemical investigations regarding the gastric juice, and for a long time after the publication of his results, the presence of free hydrochloric acid in this fluid was regarded as established: it has, however, been shown (in vol. i. p. 93) that free lactic acid is the predominating acidifying agent in the stomach.

We have already stated all that need be said regarding the comparatively rare occurrence of hydrofluoric, acetic, and butyric acids in the gastric juice, in our remarks on those acids in the first volume: we have only to add that Frerichs has recently succeeded in detecting butyric acid in the stomach of a fasting horse and of a fasting sheep, thus confirming the earlier experiments of Tiedemann and Gmelin.

In regard to the free acid in the gastric juice, I may observe that in six experiments in which I dried the gastric juice *in vacuo*, and intercepted the hydrochloric acid which was evolved (see vol. i. p. 93), I found it to vary from 0·098 to 0·132%; and I then found from 0·320 to 0·583% of free lactic acid in the residue; so that if lactic acid had been the only free acid in the gastric juice (that is to say, if the acidity had depended on that acid alone) it would have ranged from 0·561 to 0·908%.

It is not at all improbable that the quantity of free acid in the gastric juice is as variable as that of the alkali in the saliva; any one, however, who has occupied himself with experiments of this nature, will see that these numbers can only give an approximative idea regarding the quantity of acid in the gastric juice; for, independently of the circumstance that the fluid collected from a gastric fistula is never obtained in a state of entire purity, the methods adopted for exciting the flow of the secretion exert an essential influence on its constitution. The gastric juice used in my experiments was collected from three dogs at very different times, after they had fasted for twelve hours. I gave them fatty bones, and collected the gastric juice in from 10 to 25 minutes afterwards; it was only by the repetition of the process that I could gradually collect a quantity of gastric juice sufficient for analysis, so that each of the six determinations may be regarded as giving a mean result. I determined the whole amount of the free acid of the filtered gastric juice, by saturating it with carbonate of baryta, and then calculating the quantity of free lactic acid from the sulphate of baryta precipitated by sulphuric acid.

Blondlot, by some erroneous process, was induced to believe that gastric juice did not decompose carbonate of lime, and was hence led to conclude that the acid reaction of the gastric juice depended solely on the acid phosphate of lime; Dumas, Melsens, and Bernard have found that not only the carbonate but also the basic phosphate of lime is soluble in gastric juice, as also are even zinc and iron, hydrogen being simultaneously developed—properties which a solution of acid phosphate of lime does not possess.

In addition to lactic acid, the solid residue of the gastric juice contains an extraordinary quantity of *metallic chlorides,* namely, chloride of sodium with smaller quantities of the chlorides of calcium and magnesium, and traces of protochloride of iron.

On evaporating gastric juice we obtain a residue consisting of crystals of chloride of sodium, moistened with a yellowish syrupy mass, which consists principally of lactate of soda. The presence of protochloride of iron may almost always be easily recognized in strongly evaporated gastric juice by means of ferridcyanide of potassium.

Phosphate of lime is only present in small quantities in filtered gastric juice.

When the juice abounds in mucus or cells, this salt usually occurs in larger quantities, if we estimate it by the ash left by the residue.

Alkaline sulphates and *phosphates* cannot be detected in pure gastric juice; neither can *ammoniacal salts.*

For if ammonia were present, on evaporating fresh gastric juice over hydrated magnesia, and extracting the residue with alcohol, there would either be a development of ammonia (which is not observed), or hydrochlorate and lactate of ammonia would be found in the alcoholic solution; on precipitating the bases from this fluid with sulphuric acid, we find no trace of ammonia in the deposit. If, however, the ammonia were combined with the magnesia as triple phosphate, this might be readily discovered by a microscopic examination of the residue insoluble in alcohol; for even when this residue was treated with a little phosphoric acid and hydrochloric acid (perfectly free from ammonia), and the solution digested with magnesia, the triple phosphate was not formed. I can, therefore, only believe that the hydrochlorate of ammonia found by Braconnot, Tiedemann and Gmelin, and others, must have been formed during the chemical examination by the action of free hydrochloric acid on mucus or some other nitrogenous animal substance.

In addition to the mineral constituents, we also find in the gastric juice certain organic substances which, however, in consequence of the extremely small quantities in which they occur, have been very little examined; these are a substance soluble in water and in absolute alcohol (formerly known as osmazome), and a substance soluble only in water, and more or less perfectly precipitable by alcohol, tannic acid, corrosive sublimate, and the salts of lead; the latter, which seems to be a mixture of several different substances, constitutes the true digestive principle; its solution, on being boiled, certainly loses the property of effecting the characteristic change on the protein-bodies and gelatigenous substances, but does not coagulate like albumen, as was formerly supposed from experiments performed with artificial gastric juice.

The ratio in which the mineral constituents of the gastric juice stand to the organic, is a somewhat varying one; in the gastric juice of the horse, Gmelin found 1·05% of organic, and 0·55% of inorganic constituents, while on the other hand Frerichs found 0·98% of organic and 0·74% of inorganic matters; in the gastric juice of the dog Frerichs found 0·72% of organic and 0·43% of inorganic constituents, while I found from 0·86 to 0·99% of the former and from 0·38 to 0·56% of the latter.

By the term *artificial gastric juice* we understand a fluid which is obtained by treating the glandular tissue of the stomach in a peculiar manner with dilute hydrochloric acid, and which possesses the characteristic property, in common with the natural gastric juice, of converting nitrogenous articles of food into soluble, non-coagulable substances.

After Eberle[*] had shown that the gastric juice, when removed from the animal body, retains the property of inducing peculiar changes in the food, and that by digesting the mucous membrane of the stomach with extremely dilute acids, we obtain a fluid which possesses true digestive powers, it was proved by Schwann[†] that it is only the glandular structure of the stomach which possesses the property of yielding a digestive mixture with acids, and further, that corrosive sublimate throws down a precipitate from it, which possesses the digestive power in a high degree. To this substance Schwann gave the name of *pepsin.* Wasmann[‡] who investigated the subject even more fully than Schwann, demonstrated that the source of the gastric juice and of this pepsin lay in the gastric glands, which he carefully observed and described; he likewise attempted to exhibit pepsin in a purer state.

He proceeded in the following manner: the glandular layer in the stomach of the pig, which extends chiefly from the greater curvature towards the cardia, was carefully detached and washed, without being cut up; then digested with distilled water at a temperature of from 30° to 35°. After some hours the fluid was poured away, the membrane was again washed in cold

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[*] Physiologie der Verdauung. Würzburg, 1834.

[†] Pogg. Ann. Bd. 38, S. 358.

[‡] De digestione nonnulla, diss. inaug. Berol. 1839.

water, and then digested in the cold with about six ounces of distilled water, and repeatedly washed, till a putrid odour began to be developed. The filtered fluid was transparent, viscid, and without any reaction; it was now precipitated with acetate of lead or corrosive sublimate; the precipitate was carefully washed and decomposed with sulphuretted hydrogen; the pepsin was then precipitated by alcohol from the watery solution in white flocks.

The pepsin thus obtained, forms, when dry, a yellow, gummy, slightly hygroscopic mass; in its moist state it is white and bulky; it dissolves readily in water, and always retains a little free acid so as to redden litmus; it is precipitated by alcohol from its watery solution; mineral acids induce a turbidity in a solution of neutralized pepsin, which disappears on the addition of a small excess of the acid; but if there be a considerable excess of the acid, there is a flocculent deposit; it is only imperfectly precipitated by metallic salts, and not at all by ferrocyanide of potassium; it has been asserted that pepsin is coagulated by boiling, but Frerichs has shown that the coagulation is merely dependent on its admixture with albumen.

This substance possesses the converting power in so high a degree, that, according to Wasmann, a solution containing only one-sixtieth thousand part, if slightly acidulated, dissolves coagulated albumen in six or eight hours. This property of pepsin is not destroyed by alcohol; and in this respect Wasmann and Schwann coincide: it is, however, lost when the solution is boiled or carefully neutralized with potash; in both cases the fluid becomes turbid.

Almost simultaneously with Wasmann, similar experiments on the digestive principle were made by Pappenheim* and Valentin,† and subsequently by Elsässer,‡ with artificial gastric juice; and they all arrived at the same general results; but pepsin sufficiently pure for chemical analysis has never been exhibited up to the present time.

As in Wasmann's method of procedure, putrid parts and digested particles of food were always mixed with the artificial gastric juice, I§ struck upon the following method of obtaining a digestive fluid in a state of the greatest possible purity.

The stomach of a recently-killed pig having been properly

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* Zur Kenntniss der Verdauung. Breslau, 1839.

† Valentin's Repert. Bd. 1, S. 46.

‡ Magenerweichung der Säuglinge. Stuttgart, 1846. S. 68 ff.

§ Ber. d. Gesellsch. der Wiss. zu Leipzig. 1849, S. 10.

cleaned, I detached from it the portion of mucous membrane in which the gastric glands chiefly lie.

As this piece of mucous membrane still contains a tolerably thick layer of submucous areolar tissue, or of the so-called vascular coat, in which the gastric glands are in a manner imbedded, this cannot be at once employed in the preparation of the digestive fluid, since then a quantity of digested gelatinous substance would be mixed with it. This source of error cannot be entirely avoided, since in every mode of treatment heterogeneous elements of tissue will be mixed with the glandular contents. In order, however, to obtain the latter in as pure a state as possible, the piece of mucous membrane, after lying for an hour or two in distilled water at the ordinary temperature, must be gently scraped with a blunt knife or spatula; the pale greyish-red, tenacious mucus which adheres to the blade must be placed in distilled water, and the mixture must be kept at the ordinary temperature for two or three hours, being frequently shaken in the interval: a little free acid must then be added, and the mixture placed for half-an-hour or an hour in a hatching-oven at a temperature of from 35° to 38°. By this time, the fluid will be found to have lost much of its viscidity, and it is now only slightly turbid; it passes readily through the filter, in the form of a perfectly limpid fluid with a scarcely perceptible yellow tint.

These and similar artificial mixtures are of much service, as experience has indeed fully shown, in the investigation of different conditions and phenomena in relation to digestion; but they are far less suited than gastric juice discharged from the living animal for experiments having for their object to isolate as much as possible from the unessential ingredients, and to render fit for chemical analysis, the true digestive principle, or the group of substances which constitute it. If the gastric juice from the living animal be always mixed with a little saliva, that fluid interferes far less with an accurate analysis than the albumen and the different peptones in the artificial digestive fluids: and even if we could separate the albumen, the peptones would still be associated with the digestive principle, as indeed they are even with the natural gastric juice, although in a far less degree. Notwithstanding the labours of many observers, it appears by no means impossible that by repeated investigations we may so limit the digestive principle as to find a chemical expression for it, whether we can exhibit the actual substance or not. Frerichs, in his classical article on digestion, has hit upon the right line of investigation —

upon the only course which can lead to definite limits—when he precipitated the natural gastric juice with alcohol; unless too much alcohol be added, the greater part of the peptones, and also of the aqueous extractive matter of the saliva, remains in solution, as indeed does a little pepsin. The precipitate dissolves pretty freely in water, from which it is precipitated by corrosive sublimate, protochloride of tin, basic acetate of lead, and tannic acid, and in an imperfect manner by neutral acetate of lead; it does not become turbid on boiling, exhibits strong digestive properties when treated with dilute hydrochloric or with lactic acid, but, like the gastric juice, is deprived of them by boiling, by absolute alcohol, and by neutralization with alkalies; in an alkaline solution it very soon becomes putrid, and in a neutral one it seems to give rise to the formation of fungi; but when rendered acid, it remains for a very long time without suffering decomposition, exactly as natural gastric juice. Frerichs has proved that the flocks precipitated by alcohol contain sulphur and nitrogen.

We shall discuss the true sources of the pepsin, the gastric glands, and their contents, in the histologico-chemical part of this work.

C. Schmidt* has propounded a very interesting view regarding the nature of the digestive principle; he regards it as a conjugated acid, whose negative constituent is hydrochloric acid, with Wasmann's non-acid or coagulated pepsin as an adjunct, and assumes that it possesses the property of entering into soluble combinations with albumen, glutin, chondrin, &c.; according to him, it more nearly resembles ligno-sulphuric acid than any other conjugated acid, and as this becomes disintegrated into dextrin and sulphuric acid, so the *pepsin-hydrochloric acid* becomes separated at 100° into Wasmann's coagulated pepsin and hydrochloric acid, and in either case it is equally impossible to reproduce the conjugated acid from its proximate elements after their separation. On bringing the complex acid in contact with an alkali, the adjunct—the substance which has been in combination with the hydrochloric acid—is precipitated. Schmidt believes that he has ascertained that an artificial digestive mixture which has expended its solvent and digestive powers, regains them on the addition of free acid; and that when hydrochloric acid is added, the pepsin-hydrochloric acid is expelled from its combination with albumen, &c., and thus regains its former properties, while the newly added

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* De digestionis natura etc. Diss. inaug. Dorp. Liv. 1846; and Ann. d Ch. u. Pharm. Bd. 61, S. 22-24.

hydrochloric acid enters into its well-known soluble combinations with albumen, &c. By the repeated addition of hydrochloric acid, a digestive fluid or this pepsin-hydrochloric acid might preserve its digesting power for ever, unless the fluid became saturated with the dissolved substances, or the conjugated acid underwent decomposition.

Ingenious as this view of Schmidt's undoubtedly is, and singularly as it seems to harmonize with certain facts, there are other and very important facts which appear to render its correctness doubtful. The existence of this pepsin-hydrochloric acid has not been recognized by any analysis of a combination of it with a mineral base or with an albuminous substance. Although I have instituted numerous experiments regarding the quantitative relations between the digestive fluid and the substances to be digested, I cannot ascertain that there are any such proportions between the acid and the digested substance as at all accord with the ordinary acid or basic combinations of acid and base; and further, the digested substances (the peptones) separated by the acid, are altogether different from the original albumen, fibrin, casein, &c., which, however, according to Schmidt, combine in a simple manner with this complex acid, and then directly undergo solution. Further grounds for opposing this hypothesis will become apparent when we enter more fully into the consideration of the peptones.

Very little is known regarding the *abnormal constituents* which, under certain physiological or pathological conditions, may occur in the gastric juice. We know that in the normal condition, the stomach, when it is empty, is invested with a layer of mucus, which exhibits no reaction with vegetable colours. In gastric catarrh, this *mucus* accumulates in larger quantities, and on chemical examination is found to present little difference from the secretions of other mucous membranes; and, like them, it only in a slight degree possesses digestive powers on the addition of a free acid: even while in the stomach it appears in part to undergo decomposition, and subsequently, on being mixed with amylaceous or saccharine food, to enter into abnormal processes of fermentation, as, for instance, *acetic*, *butyric*, and *lactic fermentation*. The contents of the stomach then contain far more free acid than occurs in them in normal digestion. The two last-named processes of fermentation are especially promoted by the presence of fat, which gives rise to heartburn, a sensation of constriction in the throat, and vomiting; and at the same time, there is often a revulsory (antiperistaltic) motion of the intestinal tube, which causes a regurgitation of bile into the stomach, and this is an additional impediment to digestion. *Biliary matters* cannot, however, strictly speaking, be regarded as abnormal constituents of the gastric juice, since they are never produced from the same sources as that secretion; they are, however, so frequently met with, that I have made few examinations of human bodies, or even of recently killed healthy animals, in which I have not discovered biliary constituents in the contents of the stomach lying near the pyloric end.

The contents of the stomach, in *post mortem* examinations, and sometimes also the matters which are vomited in cases of gastric catarrh, are perfectly neutral or even alkaline on their outer surface, which is turned towards the walls of the stomach, while the inner parts often exhibit a very strong acid reaction; this phenomenon, wonderful as it appears at first sight, is obviously dependant on the circumstance that there must simultaneously have been a deficient secretion of gastric juice, and such slight movements of the stomach as not to have sufficiently mixed the contents with one another; and hence, either that the inner portions have undergone one of the above-mentioned acid fermentations, or that they have retained the acid reaction peculiar to the food.

It appears as if heterogeneous matters in the animal body made a repeated circulation through the gastric glands, as they seem to do through the salivary glands, before they are removed by the kidneys, or undergo change in any other part; at least this seems to be shown by the experiments of Bernard,* who injected solutions of sulphocyanide of potassium and of perchloride of iron into different veins of the same dog, and first observed the formation of sulphocyanide of iron in the gastric juice.

It is universally known that in uræmia, or after extirpation of the kidneys, *urea* is secreted by the gastric glands.

Since the time of Nysten (see vol. I. p. 166), urea has often been found in the vomited matters in cases of uræmia, consequent on Bright's disease or on cholera. Bernard and Barreswil† have made two interesting experiments in reference to this point. After extirpating the kidneys in dogs, they found that at the commencement of the retention of the urinary constituents in the blood, the gastric juice contained no urea, but a very large quan-

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* Arch. gén. de Méd. 4 Sér. T. xi. p. 310.

† Ibid. T. xiii. p. 449-465.

tity of hydrochlorate of ammonia, without, however, being less acid than in the normal state: it is worthy of notice that the gastric juice, under these circumstances, was secreted very copiously without the irritation caused by the presence of food, that is to say, when the dog was fasting. As long as the gastric juice remained acid, these chemists found no urea in the blood; they found it, however, as soon as well-marked morbid symptoms were established in the animal; and in this case there was only a little gastric juice, which, moreover, was secreted in a decidedly alkaline state, and contained much carbonate of ammonia.

In two cases in which I analysed vomited matters, I found urea when the patients presented none of the phenomena of uræmia; the vomited matter had a distinctly urinous odour, and, moreover, contained uric acid. It was afterwards proved that the patients, who were hysterical girls, had been drinking their own urine, and had simulated retention of that excretion. Rayer* has recorded a similar case. In accordance with Bernard's experiments, we very often find carbonate of ammonia in vomited matters, and especially in the contents of the stomach after death. In the group of symptoms which are associated with cholera and Bright's disease, and to which we give the name *uræmia*, I have always found the contents of the stomach and the vomited matters strongly alkaline, and always rich in carbonate of ammonia, but never containing urea. The symptoms indicating uræmia must, however, have their foundation in something more than in the mere decomposition of urea into carbonate of ammonia; for when I injected dilute solutions of carbonate of ammonia in various proportions into the blood-vessels of cats and dogs, convulsions, and even tetanic spasms (in the case of large doses) ensued, which, as is well known, do not pertain to the ordinary phenomena of uræmia, while vomiting did not occur in either class of animals, although it may be induced readily in both. The stomach was usually only slightly reddened, and presented no essential change in relation to its amount of mucus.

We are as yet unable to make any decisive statement regarding the quantity of gastric juice secreted in twenty-four hours; indeed, on this point, we are at present entirely devoid of data. We only know that, in the healthy state, its secretion is entirely dependant on the ingestion of food, and that some articles of diet excite a more copious effusion of gastric juice than others. Thus, for in-

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* Maladies des Reins, p. 285.

stance, sugar, aromatic substances, spirit of wine, and alkalies, when introduced into the stomach, immediately excite an almost overflowing secretion of gastric juice; while, on the other hand, animal substances, which remain for a longer period in the stomach, require a far greater quantity of gastric juice for their perfect conversion.

According to my experiments, 100 grammes of the fresh gastric juice of a dog cannot, on an average, effect the solution of more than 5 grammes of coagulated albumen (calculated as dry). Now if we assume that an adult man receives into the stomach about 100 grammes of albuminous matter in twenty-four hours, there must be secreted 2000 grammes, or 4 pounds of gastric juice, for the digestion of this quantity. As we shall return to this subject in our remarks on the processes of digestion and nutrition, we need not enter into it more fully in the present place.

After the preceding observations, there can be no doubt regarding the *physiological function* of the gastric juice. The gastric juice serves not merely to dissolve, but also to modify the nitrogenous elements of food, as, for instance, the protein-compounds and their derivatives. It was formerly believed that its only use was to convert insoluble and coagulated substances into the corresponding soluble matters, and thus to render them capable of resorption, and that it did not in any way affect the soluble substances. If we have since convinced ourselves that the casein is first coagulated by the gastric juice, in order again to be converted by it into a soluble substance, we yet believe that soluble albumen neither requires nor undergoes any such alterations in order to be resorbed, or, as we commonly express it, to be assimilated. (Tiedemann and Gmelin.) On the other hand, we learn, from a positive experimental inquiry, what are the products which are developed during the process of digestion; and we ascertain that, by the action of natural or artificial gastric juice on protein-bodies or gelatigenous matters, there are formed thoroughly new substances, which, although they coincide in their chemical composition and in many of their physical properties, with the substances from which they are derived, essentially differ from them, not only in their ready solubility (in water, and even in dilute alcohol), but in having now lost the faculty of forming insoluble combinations with most metallic salts. The formation of these substances, which we designate as *peptones*, depends solely on the action of the gastric juice, and occurs without the evolution or absorption of any gas, and without the production of any secondary substance.

Beaumont was the first who observed that non-coagulated albumen also undergoes a change on the stomach, while Tiedemann and Gmelin, and subsequently Blondlot, believed that they had arrived at the opposite conclusion, from their experiments. Any one may, however, very easily convince himself that the blood-serum and the albumen of eggs when stirred with water and filtered, are rendered as strongly turbid by the gastric juice as by any other dilute acid; the gastric juice, whether it be natural or artificial, often exerts little or no further influence on the albumen, when its digestive power is gone in consequence of the partial or total loss of the free acid. If, however, we again add fresh acid, we perceive the gradual conversion of the albumen in the diminution of the quantity of the coagulable substance, unless, like Blondlot, we use too small a quantity of gastric juice for the albumen; finally, the fluid ceases to give any trace of ordinary albumen, either when boiled, or on the addition of nitric acid or of any other test. The same process may be observed in natural digestion. If, for instance, we observe the contents of the stomachs of dogs with a gastric fistula, after they have swallowed such solutions of albumen, we find that the contents at first have only a slight acid reaction. (Whether they are clear, or turbid from the partial precipitation of the albumen, is a point which cannot be decided, in consequence of the invariable presence of mucus.) Very soon, however, after from 5 to 10 minutes, so much gastric juice has been secreted, that the alkali of the soluble albumen is not merely saturated, but the whole digestive mixture has assumed a strong acid reaction. Here also we may observe a gradual diminution of the coagulable matter; but I will not venture to deny that a part of the albumen may pass in an uncoagulated condition into the small intestine, in a state of health, as has been observed by Tiedemann and Gmelin. Mialhe* has also convinced himself of the metamorphosis of soluble albumen during gastric digestion. In relation to the products of the digestion of soluble albumen, I have been unable, with the means we at present possess of analysing such complex bodies as the protein-compounds, to discover any difference between the peptones of soluble and coagulated albumen.

Schwann, in accordance with the ideas and nomenclature of that day, gave the names of *osmazome* and *ptyalin* to the substances which resulted from the digestion of albumen; Mialhe was the first to discover that a single, easily soluble substance, is produced from the digestion of albumen or other protein-bodies, and

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* Journ. de Pharm. et de Chim. 3 Sér. T. 10, p. 161-167.

gave to it the name of *albuminose.* We shall return, in a future part of the work, to the properties of albumen-peptone.

The fibrin of the blood is not dissolved by the gastric juice in the same manner as by a solution of nitre (see vol. I. p. 351), but it is converted into a non-coagulable, soluble substance, *fibrin-peptone.*

That soluble casein is coagulated in the stomach before it undergoes the actual process of digestion, has been long known; it being proved by observing milk which has been vomited, and by the well-known property of the calf's stomach (rennet) to induce coagulation. More recent observations have only shown that the casein thus coagulated requires in general a longer time for its solution than most other protein-bodies, and that here also as in the other bodies of this class, the more easy or difficult digestibility principally depends on the atomic grouping in which it is secreted; hence, according to Elsässer,* the casein of woman's milk, which only coagulates into a sort of jelly, is more easily digested than the clotted and more firmly coagulated casein of cow's milk.

Globulin, vitellin, legumin, and other protein-bodies, behave, according to my experiments, both in natural and artificial digestive fluids, precisely the same as albumen.

It is singular that glutin, chondrin, and gelatigenous tissues, during their digestion in the stomach, are converted into substances which, in their physical and in most of their chemical properties, perfectly correspond with the peptones of the protein-bodies. The degree of the solubility of these substances is however essentially dependant on mechanical relations; actually formed gelatine is more readily changed than areolar (cellular) tissue, and the latter far more quickly than tendon and cartilage; indeed, as a general rule, the latter do not remain in the stomach sufficiently long to be completely digested, but for the most part are carried away undigested with the excrements.

We shall treat of the digestibility of mixed food and of the individual animal tissues, when we consider the digestive process generally.

Very little attention has hitherto been paid even to the best-known peptones; indeed, until Mialhe published his researches, positively nothing was known regarding their physical or chemical relations. This chemist erroneously regarded the soluble substances produced by digestion from the protein-bodies and from

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* Die Magenerweichung der Säuglinge. Stutt. u. Tüb. 1846.

the gelatigenous tissues as perfectly identical. The following properties, which Mialhe attributes to his albuminose, are certainly correctly observed, and are common to most of the peptones; in the solid state the digested substances are white or of a pale yellow colour, possess little taste or odour, and dissolve readily in water and slightly in spirit, but not at all in absolute alcohol. The watery solutions of these substances are not precipitated by boiling, by acids, or by alkalies, but deposits are thrown down by metallic salts, by chlorine, and by tannic acid.

My own observations lead me to the belief that all the peptones are white, amorphous bodies, devoid of any odour, and having merely a mucous taste, soluble in every proportion in water, and insoluble in alcohol of 83%; their watery solutions redden litmus; they combine readily with bases—with alkalies as well as with earths—so as to form neutral salts, which are very soluble in water. The aqueous solutions of these salts are only precipitated by tannic acid, corrosive sublimate, and, if caustic ammonia has been previously added, by acetate of lead; all other metallic salts, even nitrate of silver and alum, produce no precipitate, and even basic acetate of lead only induces a slight turbidity, which disappears on the addition of an excess of the test. No precipitation or turbidity is produced by the addition of mineral or organic acids, either in a concentrated or in a very dilute state; even chromic acid fails to produce any appreciable effect. The ferrocyanide and ferridcyanide of potassium, when added to solutions acidified with acetic acid, occasion only a slight turbidity.

I have been unable to obtain the peptones perfectly free from mineral substances: I have, however, obtained them free from phosphates and hydrochlorates, so that their ash contained only alkaline carbonates or carbonate of lime, with small quantities of alkaline sulphates. With regard to the quantity of sulphur in the peptones, I found it to be constantly the same as that in the substances from which they were derived; thus, for example, in the peptone of the albumen of eggs, after deducting the alkali or lime, I found in three experiments, 1·579, 1·659, and 1·600% of sulphur, the mean being 1·602%, which coincides almost to the very decimal places with Mulder's determination of the amount of sulphur in the albumen of the egg. This sulphur appears, however, to be contained in the peptone, in precisely the same form as it exists in the albumen; at all events, when treated with alkalies it yields very distinct indications of sulphur, both with the salts of lead and with silver-foil. In my repeated analyses I have been unable to detect any differences between the quantities of nitrogen, carbon, and oxygen, contained in the peptone and in the substance from which it was derived, nor can I infer from my quantitative results, that the conversion of the protein-bodies into peptones is accompanied by an assimilation of water, as might have been supposed. The metamorphosis may be appropriately compared with that of starch into sugar, or even better perhaps, with that of cholic (Strecker's cholalic) acid into choloidic acid.

I have prepared the peptones either from the natural gastric juice of dogs or from artificial digestive fluid obtained from the pepsin-glands of the stomach of the pig and from coagulated albumen, fibrin, casein, legumin, glutin and chondrin in a state of extreme purity, by allowing them to remain in contact at the necessary, somewhat elevated temperature, till the greater part of the substance to be digested had dissolved; the whole mixture was then boiled and filtered; the acid fluid was somewhat evaporated over carbonate of lime, and after a second filtration, was concentrated to the consistence of honey. The addition of alcohol (of 83%) precipitated the lime-and-peptone compound, but dissolved the chloride of calcium; the undissolved portion, which was very hygroscopical on exposure to the air, and soon ran into a varnish-like mass, was now boiled with absolute alcohol, and was finally extracted, while still hot, with ether containing alcohol. The alkali-compound admitted of being easily prepared from the lime-compound by means of alkaline carbonates. The peptones were obtained nearly, but not perfectly, free from mineral constituents, by carefully removing the baryta, or a great part of it, from their baryta-compounds, by means of sulphuric acid.

The alkaline carbonates only partially remove lime from the lime-peptone, but they entirely free it from phosphate of lime; if, for instance, the alkaline peptone-solution after being freed by filtration from the carbonate of lime thrown down by carbonate of potash, be slightly acidified with acetic acid, evaporated and freed from acetates by extraction with alcohol, neither carbonate of soda nor ammonia produces any precipitate when added to the aqueous solution, but a precipitate is caused by oxalate of ammonia; the ash consists here almost entirely of carbonate of lime. Thus albumen-peptone contains, for instance, 5·53% of lime. Hence the saturating capacity of albumen-peptone = 1·67, and its atomic weight = 5960.

I have obtained perfectly similar results in analysing other peptones, the details of which I shall describe more fully in another part of this work; this much, however, may be concluded with certainty, that the digestion of the protein-compounds is something more than a simple formation of the well-known hydrochlorate of albumen, as was formerly supposed, and as has partly been assumed by Schmidt, in the hypothesis to which we have previously referred.

The following facts are worthy of notice in reference to the *digestive power* of the gastric juice: it is *suspended* by boiling, by saturating the free acid with an alkali or even with phosphate of lime, by sulphurous, arsenious, and tannic acids, by alum and by most metallic salts; and it is very much *impeded* by the addition of alkaline salts, or by saturating the fluid with peptones or other organic substances, either nitrogenous or non-nitrogenous. The addition of *water* to a gastric juice which has been already saturated by a peptone, enables it to digest an additional quantity of protein-substances; the digestive power is also restored to a certain degree by the repeated addition of *free acid.* Too much free acid without due dilution with water, entirely suspends the digestive power. The most favourable ratio of the free acid of the gastric juice is when 100 parts of the latter are saturated by about 1·25 of potash. Hydrochloric and lactic acids are the only acids which yield energetic, active digestive fluids with pepsin; sulphuric, nitric, and acetic acids yield with pepsin a digestive mixture of only slight power; while phosphoric, oxalic, tartaric, and succinic acids can in no degree replace the lactic or hydrochloric acid in the process of digestion. Fats, when added in certain quantities to the gastric juice, promote the conversion of the protein-compounds into peptones.

It need excite no wonder that sulphurous, arsenious, or tannic acid should suspend the digestive power of the gastric juice, for it is well known that these substances check other metamorphoses, and especially the phenomena of fermentation. Taking into consideration the chemical properties of pepsin, and its power of combining with metallic salts and other substances, we could hardly expect that the above-named substances would exert any other effect on the digestive power of the gastric juice.

Wasmann has very clearly shown that no digestion is possible unless the gastric juice contains a free acid; indeed he was led to the view that the digestive power resides "in solo acido." This latter view is, however, sufficiently controverted by the experiments of numerous observers; we need, for instance, only refer to those of Blondlot, who believed that he had shown that the peptones are bodies which are essentially different from the soluble hydrochlorates and lactates of the protein-compounds. The simplest experiment is indeed sufficient to show that dilute acids are incapable of producing the same effects as the gastric juice.

It was shown by Elsässer[*] that a digestive mixture which had been already saturated with a digested substance, and had consequently lost its digestive powers, regains them in part, either by being diluted with water, or by the addition of free acid. Different views have been founded on these experiments (as, for instance, by Elsässer and Schmidt), but it appears to me that questions of this nature can only be decided by quantitative determinations; and I[†] have instituted many series of experiments in reference to this point, without, however, as yet succeeding in obtaining a definite formula for these relations, which could be expressed in numbers.

Elsässer, from his experiments with an artificial digestive fluid, concludes that from 3 to 4% of hydrochloric acid, HCl.HO, (and, therefore, probably from 1·2 to 1·6% of the anhydrous acid, HCl,) is the most favourable ratio; besides this, the quantity of solid constituents in it should not exceed 1·25%.

Wasmann, and other observers, for the most part ascribe the peptic force to the free acid in general. My numerous experiments have, however, led me to the result which I have already mentioned, namely, that other acids when associated with pepsin, possess only a slight digestive power, and that even hydrochloric acid in which phosphate of lime had been dissolved to the saturating point, no longer possesses any digestive force when united with pepsin.

Very different views were formerly deduced from the results of positive investigation, in reference to the activity of the alkaline chlorides in digestion. I myself[‡] formerly believed that I had ascertained that the addition of chloride of sodium to the gastric juice, promoted the solution of the protein-bodies, but more recent and extensive experiments have convinced me that every kind of neutral alkaline salt very much impedes the digestive process.

It is easy to demonstrate,[§] by experiments on living animals, and with both artificial and natural gastric juice, that fat very much promotes the conversion of the protein-bodies into peptones. This observation has been confirmed by Elsässer.

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[*] Op. cit.

[†] Ber. der Ak. der Wiss. z. Leipz. 1849, S. 8-50.

[‡] Op. cit.

[§] Simon's Beiträge. Bd. 1, S. 22.

The experiments of most observers agree in showing that the gastric juice exerts no perceptible action on the ordinary *non-nitrogenous foods.* The fats may certainly, as we have already mentioned, exert an influence on the gastric digestion, but they undergo no recognizable chemical change. Starch, gum, and sugar, when placed in pure gastric juice at the temperature of the animal body, do not undergo any change corresponding to the digestion of nitrogenous bodies. We shall return to the consideration of mixed and natural vegetable food when we treat of the process of digestion.

If the fats exert an influence on digestion, we can hardly conceive that this action is due to mere contact, and that it is unaccompanied by any change in the fat itself, but the quantity of fat which acts and is modified in this way in the digestive process, is so minute as not to be appreciable in our analyses; it is evident that it is not in the stomach that the fats are digested.

We have already mentioned (see p. 37) that Bernard believed that he had discovered that acid saliva, like acid gastric juice, digests animal food, and that alkaline gastric juice, like alkaline saliva, digests starch; this view is, however, opposed by the positive experiments of Mialhe and Jacubowitsch. I have also convinced myself that neither natural or artificial gastric juice, even when rendered strongly alkaline, exerts any action on starch. According to Jacubowitsch, saliva mixed with gastric juice converts starch into sugar; and I have confirmed this experiment with acid, neutral, and alkaline mixtures.

As the vegetable substances are permeated by saliva and gastric juice, we find that they are softened and partially loosened in their texture in the stomach; the gastric juice here naturally exerts its digestive power only on their nitrogenous constituents, while the non-nitrogenous materials probably only undergo a preparation in the stomach for the changes which are normally effected in the small intestines.

Pure gastric juice antagonises the ordinary processes of fermentation, and hence lactic, acetic, and alcoholic fermentation are excluded from the sphere of gastric digestion, so long as this process is a normal or physiological one. At the very most only a part of the cane or milk sugar introduced into the stomach can be converted into glucose.

BILE.

The bile of different animals does not present exactly the same physical properties; in the following points, however, we find a tolerable identity of character between the different kinds of this secretion. When derived from the gall-bladder, the bile occurs as a mucous, transparent fluid, capable of being drawn out in threads, of a green or brown colour, of a bitter but not astringent taste and sometimes leaving a rather sweet after-taste, and of a peculiar odour, which, when the bile is warmed, often vividly reminds the observer of musk. Its specific gravity is about 1·02: bile does not diffuse itself readily through water, unless the mixture be stirred; it is usually weakly alkaline, often perfectly neutral, and only in disease, and then rarely, acid. Bile in its ordinary state, before its mucus is removed, putrefies very readily, but when it is freed from mucus, putrefaction is not easily induced.

Fresh human bile can only be obtained from the bodies of criminals immediately after their execution; the bile of animals is commonly obtained from the gall-bladder immediately after they have been killed; in the case of animals like the stag and the roe, which possess no gall-bladder, it is only rarely that we can obtain from the larger biliary ducts a quantity of bile sufficient for an accurate analysis. With the view of more accurately studying the relations of the biliary secretion and its influence on digestion, Blondlot,* Schwann,† and C. Schmidt‡ have established biliary fistulæ in animals. These fistulæ are made in the same way as gastric fistulæ, by cutting through the abdominal walls, but the incision in this case must be somewhat longer; we then raise up the lower border of the left lobe of the liver, and search for the ductus choledochus at the point where it opens into the duodenum; if the animal has a gall-bladder, the best plan is to tie the above-named duct at two spots and to cut away some of the intervening portion; all the bile must then flow through the cystic duct into the gall-bladder. The latter must then be separated as well as possible, and as far as is necessary, from its attachment to the liver, and drawn forth from the abdominal cavity, while any pro-

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* Essai sur les fonctions du foie et de ses annexes. Paris, 1846.

† Müller's Archiv. 1844. S. 127-162.

‡ Buchheim's Beitr. z. Arzneimittellehre. Leipz. 1849. S. 116.

lapsed intestine must be returned, and the wound, as when we establish a gastric fistula, closed by strong twisted sutures; an incision must then be made into the gall-bladder, and the outer edges of the wound secured, as in the case of the stomach. After this operation, which is far the more severe of the two, animals much more frequently die from peritonitis and enteritis, than after the establishment of a gastric fistula. If we make the ductus choledochus open directly on the external surface of the body, the prognosis is still more unfavourable, since the canal becomes attached with less facility and certainty to the abdominal walls. It is advisable to introduce a small glass tube or a silver canula into the duct immediately after the operation, in order to prevent the bile from coming in contact with the lips of the wound.

Physiologists have ever held the most different and opposite views regarding the function of the liver and of its secretion, and even at the present day the subject is involved in the greatest obscurity; and in regard to the nature of the bile itself, since zoochemical analyses of it were first attempted, there have been so many difficulties and impediments in the way of prosecuting them, that it is only during the last few years that any light has been thrown upon this most obscure of all the departments of animal chemistry. The most distinguished chemists of our time, founding their views on the most exact experiments, have been led to perfectly different results regarding the constitution of the bile; we shall, however, consider it in the following manner, which is based on the most recent investigations conducted under Liebig's auspices, and explains many of the former points of difference:

Every kind of bile contains two essential constituents, namely, a resinous and a colouring constituent.

The *resinous constituent* is, as a general rule, the soda-salt of one of the *conjugated acids* described in vol. I, pp. 222-235, whose adjunct is *glycine* or *taurine*.

The *colouring principle* of the bile has also been described in vol. I, pp. 312-318: it occurs in combination with an alkali in the bile.

A third never-failing constituent is the *cholesterin* described in vol. I, pp. 272-279.

Besides these essential constituents, we also find *fats* and combinations of the alkalies with *fatty acids* in the bile.

Moreover, we find in the bile the same *mineral salts* which occur in most other animal fluids; namely, chloride of sodium (the principal salt), a little phosphate and carbonate of soda phosphate of lime and magnesia, and extremely minute quantities of iron and manganese, but no alkaline sulphates. No salts of ammonia are found in fresh healthy bile. The relation of the potash and soda in the bile of different animals—a fact noticed by Bensch, but more prominently evolved by Strecker — is deserving of careful attention: the bile of salt-water fishes contains almost exclusively potash-salts, while that of the herbivorous mammalia contains almost exclusively soda-salts; whereas from the nature of the food of the animals, we should have expected to have met with the opposite result. We have already alluded to the presence of copper in the bile. (See vol. I, p. 451.)

Finally, a greater or lesser quantity of *mucus* always occurs in the bile. This, like other varieties of mucus, is mixed with numbers of epithelial cells; here, however, the mucus-juice very much preponderates over the epithelium.

Fresh normal bile contains no morphological elements except the cells of cylindrical epithelium thrown off from the mucous membrane of the biliary ducts and the gall-bladder; these cells often remain grouped together in their natural arrangement.

It is needless to introduce in this place any historical sketch of the manifold experiments and views which have been adduced in reference to the composition of the bile, since they are described with more or less minuteness in all our text-books of Animal Chemistry, and in every monograph on the bile, and since they do not throw the slightest light on the complex nature of this fluid and of its constituents. In reference to the writings of Berzelius, it seems, however, necessary to state, that according to his view, which has very recently been defended by Mulder, the most essential constituent of the bile is not an acid in combination with soda, but an indifferent substance named *bilin,* which in its decomposition gives rise to those substances which were formerly described by Gmelin, and subsequently by Demarçay and others, as occurring in the bile. Any one who carefully studies the chemical characters of taurocholic acid (the choleic acid of Strecker), and compares them with those which are ascribed by Berzelius to his bilin, will readily detect the causes of the error by which that chemist was led to assume the existence of an indifferent bilin; and they will no longer wonder that all who have repeated the positive experiments of Berzelius have quite as thoroughly confirmed them, as those which were instituted by Liebig and his pupils, but led them to a different view of the subject.

If these disputes amongst the first chemists of our time, regarding the constitution of the bile, should at the first glance cause the faith of the physician in the extreme certainty of chemical investigation to stagger, and should blight his hopes of our ever attaining to an exact humoral pathology, let him carefully study the grounds of these differences of opinion, and he will be convinced that he has no cause for doubting the accuracy and certainty of chemical inquiries. He must especially bear in mind that different chemists have entered upon the study of this complex fluid from different points of view, without, as it were, meeting one another half-way, and thus obtaining a general survey; further, it must be recollected that the bile undergoes decomposition with extraordinary rapidity, and scarcely any chemist assumes that he has employed perfectly undecomposed bile in his analyses; indeed it has even been believed that the decomposition of the bile commences within the healthy living body in the gall-bladder. Moreover it is clear that by employing different methods of analysis, we obtain different products of metamorphosis. Finally, we must always recollect that the comprehension of the results of the analysis—the consideration of the objects perceived—is always subjective, that is to say, it is the result of an intellectual process. Hence we see that even where all the facts were fully confirmed, none of the opinions that have been expressed regarding them have preponderated, since none of them could be made to harmonize with all the results of different experimenters. This object has, however, been attained, as we already observed in the first volume, by means of Strecker's experiments, conducted under the auspices of Liebig, although, as might be expected, there still remain some few obscure points requiring further elucidation.

In reference to the resinous acids of the bile, we have little to add to what we have already communicated regarding Strecker's investigations. Mulder,* however, still defends the opinion of Berzelius, that bilin is secreted by the liver, but believes that it undergoes a complete decomposition in the gall-bladder. Strecker,† on the other hand, has extended his investigations, and has analyzed the bile of various classes of animals; and hitherto he has found that the only difference in the composition of the bile of different animals is in the varying proportions in which the taurocholic and glycocholic acids (the choleic and cholic acids of Strecker) exist in them. In the bile of fishes (*Gadus morrhua, Pleuronectes maxi-*

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* Scheik. Onderz. D. 5, p. 1-104.

† Ann. de Ch. u. Pharm. Bd. 70, S. 149-198.

mus, Esox lucius, Perca fluviatilis), Strecker found that the resinous constituents consisted almost entirely of alkaline taurocholates, with mere traces of alkaline glycocholates; and, singularly enough, that the potash-salts preponderated in the salt-water, and the soda-salts in the fresh-water fishes. The researches of Strecker show that the bile of the dog contains almost exclusively taurocholate of soda, and a similar fact had been previously ascertained by Schlieper in reference to serpents' bile. It seems, moreover, to follow from Strecker's experiments, that the nature of the food (in the case of dogs) exercises no influence on the composition of the bile. The bile of the sheep contains, according to Strecker, a mixture of much taurocholate of soda with a comparatively small amount of glycocholate. The bile of the goose, according to Marsson's investigations, contains almost exclusively taurocholic acid. Hyocholic acid has only been found in the bile of the pig; on the other hand, it appears that the small quantity of sulphur formerly detected by Strecker and Bensch in the bile of the pig depends on the presence of a hyocholeic acid; that is to say, that besides the glycine-yielding hyocholic acid (glycohyocholic acid), there also occurs a taurine-yielding acid in very small quantity—an acid in which the taurine is united with the same resinous acid ($C_{50}H_{40}O_8$, the hyocholalic acid of Strecker) with which glycine is combined in hyocholic acid. The products of the decomposition of hyocholic acid have been carefully studied by Strecker. It is worthy of notice that this chemist, in examining pigs' bile from which the biliary acids had been removed by hydrochloric acid, discovered a very strong sulphurous base, which is capable of combining even with carbonic acid.

The peculiar pigment has never yet been found to be absent in the bile of any animal. In the bile of carnivorous and omnivorous animals, including man, we have a brown pigment, the cholepyrrhin of Berzelius; while in the bile of birds, fishes, and amphibia, we usually find an intense green pigment, biliverdin. The brown bile-pigment is moreover never contained in a state of freedom, but is always in combination either with soda or lime; in the latter case it is insoluble, and may be easily recognized in the brown granules which we sometimes observe in examining the bile with the microscope. A microscopico-chemical analysis affords a ready proof that these granules consist of the combination of cholepyrrhin with lime.

The quantitative relations of the biliary constituents have not as yet been very accurately investigated; the following statements may, however, be regarded as representing with tolerable accuracy the mean composition of the bile.

Normal *human bile* contains, according to the determinations of Frerichs,* about 14%, or a little more, of solid constituents; ox-bile, from 10 to 13%; and pigs' bile (according to Gundelach and Strecker†) from 10·6 to 11·8%; the amount of water may, however, be as variable in the bile as in most other animal secretions.

Gorup-Besanez‡ found 9·13% of solid constituents in the bile of an old man, and 17·19% in that of a child aged twelve years; but whether the bile is always more diluted in old age than in childhood, is a question that must be decided by further investigations.

The organic constituents of human bile amount to about 87% of the whole solid residue; and much the same ratio seems to obtain in the bile of animals.

Berzelius obtained 12·7% of ash from the residue of ox-bile; and Bensch§ 13·15% from that of calves' bile, 11·86 from that of sheeps' bile, 13·21% from that of goats' bile, 13·6% from that of pigs' bile, 12·71% from that of foxes' bile, 10·99% from that of fowls' bile, and 14·11% from that of the bile of fresh-water fishes.

The alkaline taurocholates and glycocholates constitute by far the greater part of the organic constituents, and amount to at least 75% of the whole of the solid constituents of the bile.

The investigations of Bensch and Strecker show that the bile of most of the animals included as yet in their experiments, contains a preponderating quantity of taurocholate of soda. As taurocholate of soda ($Na\,O.C_{52}H_{44}NO_{13}S$) contains 6% of sulphur, we may readily estimate the taurocholic acid contained in any quantity of bile, from the amount of sulphur contained in the portion soluble only in alcohol. Schlieper‖ found 6·2% of sulphur in purified serpent's bile, that is to say, in its alcoholic extract; in that of the dog, Bensch found 6·2%, but Strecker only 5·9%; in that of the fox, Bensch found 5·96%; while in that of the sheep, Strecker found from 5·7 to 5·3%. Hence we perceive that the bile of these animals contains taurocholic acid almost exclusively, while ox-bile, whose alcoholic extract contains only 3% of sulphur, con-

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* Hannov. Ann. Bd. 5. H. 1 u. 2.

† Ann. d. Ch. u. Pharm. Bd. 62, S. 205-232.

‡ Untersuch. über die Galle. Erlangen, 1846, S. 44.

§ Ann. d. Ch. u. Pharm. Bd. 65, S. 215.

‖ Ibid. Bd. 60, S. 109.

tains taurocholic and glycocholic acids in nearly equal proportions. As the bile of the pig contains only from 0·3 to 0·4% of sulphur, we may hence draw our conclusions regarding the small quantity of hyocholeic or tauro-hyocholic acid contained in it.

No correct determinations have been made regarding the amount of the pigment, the cholesterin, or the fats and fatty acids in the bile.

Moreover, the quantitative determinations of the mineral constituents of the bile, cannot be regarded as altogether trustworthy; the only established fact seems to be that there is a quantity of soda or potash present which is equivalent to the resinous acids; but the pigment and the fatty acids are also combined with alkalies; ordinary analyses of the ash, and even those made in accordance with Rose's directions, do not by any means lead to the result that all the alkali combined with organic matter has been accurately determined. The ash of ox-bile is almost the only one which has been carefully examined; it contains, according to Weidenbusch,* 27·70% of chloride of sodium, and about 16% of tribasic phosphate of soda, with only 3·025% of basic phosphate of lime, 1·52% of basic phosphate of magnesia, 0·23% of peroxide of iron, and 0·36% of silica.

I have convinced myself that the bile—at all events, that ox-bile—contains pre-formed *alkaline carbonates*, by the same experimental proof which I adopted to demonstrate the presence of these salts in fresh blood. If we place bile under the receiver of an air-pump, and abstract the air till the fluid appears to boil, and if we then add acetic acid to the bile thus freed from gas, and again form a vacuum around it, very large quantities of carbonic acid will be evolved, even with the first strokes of the pump.

I must here remark that, in performing this experiment, perfectly fresh bile, from which the mucus had been removed by alcohol, was employed; and this, on the addition of acetic acid, yielded no precipitate of fine granules which might have facilitated the formation of vesicles of aqueous vapour. The experiment may also be easily performed by simultaneously placing acidified and non-acid bile *in vacuo*, when the difference more readily strikes the eye. In 100 parts of fresh ox-bile, I found, in two quantitative determinations, 0·0846, and 0·1124 parts of the simple carbonate of soda.

We must here further remark, in connexion with the uncertainty of ash-analyses, that the soda combined in the bile with

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* Pogg. Ann. Bd. 76, S. 386.

organic substances, will appear in the ash as carbonate of soda; this, however, occurs only in extremely small quantity, for the greater part of the soda is saturated by the sulphuric acid which is formed during the combustion of the taurocholic acid and the mucus. The sulphuric acid in the ash, resulting from this source, is, however, extremely variable, according to the mode in which the incineration has been conducted. Weidenbusch, who employed Rose's method for the determination of the ash, satisfied himself that, even in this way, a great part of the sulphur contained in these organic substances has volatilized, and therefore does not appear in the ash as sulphuric acid. The researches of all the more recent chemists show that fresh bile contains scarcely a trace of sulphuric acid. A portion, however, of the soda which was in combination with organic substances, is found in the ash as phosphate of soda, a salt which—as ordinary phosphate of soda ($2\ NaO.\ HO.\ PO_5$)—most probably exists pre-formed in the bile. Thus it is easy to see that, under certain conditions, even no carbonate of soda may be found in the ash.

In normal human bile, Frerichs* found from 0·20 to 0·25% of chloride of sodium, and an equal quantity of phosphate of soda. Theyer and Schlosser found 3·56% of this salt in the bile of the ox.

The determination of the *mucus* in normal bile is not to be depended on, for the bile which has been examined has usually been expressed from the gall-bladder with such force that a large quantity of the epithelium, from the lining membrane of that organ, becomes mixed with the secretion. In ox-bile I found only 0·134, and in human bile 0·158% of mucus, when I used every precaution to avoid this source of error.

Very little is known regarding the changes which the bile undergoes under purely physiological conditions. When it has been retained for a long time in the bladder, as, for instance, in cases of prolonged fasting, it is concentrated. A highly nitrogenous diet not only increases the biliary secretion, but likewise renders it more concentrated than ordinary bile.

As in the case of other secretions and excretions, *heterogeneous constituents* may find their way into the bile. The older writers have often asserted that the bile contained *albumen*, but they doubtless mistook mucus for albumen. Albumen is, however, sometimes found in the bile, especially in fatty liver (although rarely), in Bright's disease, and in the embryonic state. In a five-

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* Op. cit.

months' human embryo I found no true bile in the gall-bladder, but only yellow coloured albumen and mucus.

Thénard has observed and described a peculiar form of albuminous bile, which was perfectly colourless; it occurred in certain cases of fatty liver. Frerichs directs attention to the film which is often formed on the surface of morbid bile during evaporation; but this membrane may be formed by the coagulation of mucus-juice as readily as by casein-like substances; in two cases of fatty liver I believe, however, that I actually found albumen, for I treated the bile with acetic acid as long as any precipitate (consisting of mucus, and biliary and fatty acids) continued to be thrown down, and then boiled the filtered fluid with hydrochlorate of ammonia, (see vol. i. p. 334); a coagulum was then formed, which yielded the ordinary reactions of the protein-bodies. Bernard* was the first who detected albumen in the bile in Bright's disease. When the bile contains pus, as is sometimes the case in abscesses of the liver, albumen must obviously be present.

In a case of obliteration of the cystic duct, in consequence of which *hydrops vesicæ felleæ* (as it has been termed) was developed, I found that the colourless fluid in the gall-bladder contained traces of coagulable matter, in addition to epithelium and mucus-juice.

The occurrence of *urea* in the bile after extirpation of the kidneys has been already noticed (see vol. i. p. 166); this substance has also been found in the bile in Bright's disease and in cholera.

The alcoholic extract of the bile of a man who died with the symptoms of fatty degeneration of the kidneys, was extracted with aqueous ether; the ethereal extract, when treated with nitric acid, yielded most distinct crystals of nitrate of urea; fat-globules were also present in it. Stannius and Sthamer† failed in detecting urea either in the bile or in the kidneys of animals whose kidneys had been extirpated.

Bizio once discovered a dark red, non-bitter bile in a patient suffering from icterus; it contained an *emerald-green pigment*, to which he gave the name of *erythrogen*, from its volatilizing at 40° and giving off a red vapour.

I found a similar substance in a case of acute yellow atrophy of the liver; its behaviour was precisely the same as that of Bizio's erythrogen; it was insoluble in water and ether, partially soluble in alcohol, but dissolved readily in concentrated mineral acids

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* Bouisson, de la bile, de ses variétés physiologiques et de ses altérations morbides. Montpellier, 1843.

† Arch. f. phys. Heilk. Bd. 9, S. 201-219.

without any change of colour. I obtained it, like Bizio, by diluting the bile with water; the insoluble portion was boiled with water, upon which a fatty green mass separated on the surface, which had the above-named properties in common with erythrogen.

In the bile of a child who died suddenly, I* found a considerable quantity of *sulphide of ammonium.*

It is sufficiently obvious that this *sulphide of ammonium* had not been separated from the blood by the liver; the only singularity is, that it should have been found in such large quantity in the bile, when the examination was made sixteen hours after death. Unfortunately nothing was known of the previous history of the case.

With the exception of the above-mentioned changes, the only other alterations in morbid bile (which can obviously only be obtained from the body after death), are of a quantitative nature in reference to the individual constituents, or are represented by modifications of the pigment. The bile has been found to be poor in solid constituents in persons who have died from severe inflammatory affections, especially from pneumonia, and likewise in fatal cases of dropsy; it is even more aqueous and attenuated in certain cases of typhus; and in diabetes there is always an excess of water. In tuberculosis the bile is very frequently, although not invariably, poor in solid constituents.

In cases of tuberculosis, Gorup-Besanez usually found the bile of the ordinary consistence; but Frerichs always found it attenuated, unless when the tuberculosis was complicated with fatty liver. This difference may be readily accounted for; Frerichs probably analysed bile in cases in which an anæmic condition had been induced, in consequence of abundant effusion (as, for instance, where diarrhœa had been excited by intestinal ulceration, or where there had been pleural or peritoneal dropsy; his last case was one of obsolete tubercle). Again, no one who has examined the blood of tuberculous patients before and after the exudation has been thrown off, can wonder that the bile should present a thin liquid appearance after an attack of acute tuberculosis. In tuberculosis combined with fatty liver, Frerichs, like Gorup-Besanez, found the bile dense, since in this condition the blood is less poor in solid constituents, and the hepatic affection is itself opposed to a copious secretion of dilute bile. Both chemists found the bile very diluted and scanty in typhus; the bodies from which the bile was obtained, were those of persons in whom

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* Schmidt's Jahrbücher der ges. Med. Bd. 25, S. 16.

the morbid process was already localised, or when death was induced, as it frequently is, not directly by the typhus, but by the subsequent anæmia. In two cases of typhus, in which the *plaques* in the intestine were only just recognizable, I found the bile dense; and every pathological anatomist must recollect cases in which the bile was tough and consistent, and, therefore, rich in solid constituents in persons who had died from typhus. In every case Frerichs found from 93 to 96$\frac{0}{0}$ of water in the bile, and Gorup-Besanez for the most part a somewhat smaller quantity.

The *solid constituents* are commonly *increased* in those abdominal diseases in which the motion of the blood in the larger veins is impeded, and where, as in certain cases of heart-disease, the blood accumulates in excessive quantity in the portal vein and the hepatic vessels. The motion of the blood in the hepatic capillaries is (as we know from physiological researches) so torpid, that if there be any impediment, as, for instance, disease of the heart, to the passage of the blood in the *vena cava,* and any check to the escape of the blood from the liver through the hepatic veins, an almost entire stagnation of the blood-current in the liver must ensue.

In cholera we also find the bile dense, tough, and consistent; this condition is likewise due for the most part to mechanical conditions; the blood of cholera patients is so tenacious and thick, that even in the vicinity of the heart it moves slowly, and thus causes a disturbed state of the circulation generally; and this effect is the more striking in the hepatic circulation, when, moreover, in consequence of the blood being deficient in water, a less aqueous bile must be secreted.

The *mucus* is often relatively increased when the bile is very dilute; indeed, in typhus we sometimes find little else in the gall-bladder than mucus, the resinous constituents being almost entirely or altogether absent; and the same is observed in catarrh of the biliary ducts.

In the absence of quantitative determinations, we cannot decide whether the separation of *crystals of cholesterin*, which we can sometimes observe with the microscope in morbid bile, is associated with an absolute augmentation of this lipoid. Gorup-Besanez has only occasionally observed this phenomenon in very concentrated bile.

Free fat is always present in the bile, but is held in solution by the taurocholic acid; occasionally, however, in examining morbid bile by means of the microscope, we may detect fat-globules, which we must be careful not to confound with the globules of separated biliary acids, which are often observable. Gorup has found fat-globules in the bile of persons who had died from typhus and from tuberculosis (in the colliquative stage). We have already alluded to the fact (see vol. i. p. 253), that in such cases free fat also passes into the urine.

It is very seldom that the bile has been found to have an *acid* reaction, and in none of these cases has it been carefully analysed.

Solon, Scharlau, and Gorup-Besanez occasionally found the bile acid in typhus; this may, however, depend partly on the spontaneous decomposition of the bile, and the consequent liberation of its resinous acids, and partly on the fact that pus is effused into the gall-bladder; for, as we shall subsequently show, this fluid, when contained in an enclosed space, often becomes acid with great rapidity.

According to Solon, the bile is sometimes as acrid as chlorine, and *bleaches litmus.* I believe that I have observed two cases of the kind which probably led Solon to adopt this view; this bile certainly decolorized litmus paper, so that it remained neither blue nor red, but its colouring matter was so dissolved out, or covered by the yellow pigment of the bile, that the original tint seemed wholly to have disappeared; in a less degree this is the case with every specimen of bile.

The following may be regarded as the simplest method of *analysing the bile.* We treat the fluid with half its volume, or from that to its own volume, of spirit (83$\frac{0}{0}$). This generally only throws down mucus, which carries with it any epithelium that may be present; we rince the precipitate first with spirit, and then with water, and dry and weigh it. The bile thus freed from mucus, is deprived of its water, by being placed first on the water-bath, and, subsequently, under the air-pump on a sand-bath heated to 100°; the high temperature in this process of desiccation is less necessary for the purpose of effecting the drying quickly than for converting the residue of the bile by the rapid evaporation of the water into a porous spongy, puffy substance, which admits of being extracted by the ordinary menstrua with comparative facility. As the residue of scarcely any other animal fluid attracts moisture so readily from the air, especial care must be paid to the weighing of its solid constituents; after the mass has cooled *in vacuo,* air from which the aqueous vapour has been extracted by chloride of calcium must be drawn into the receiver, and the weighing must be completed as quickly as possible. The residue must then be extracted with anhydrous ether, a process requiring much time, because we cannot pulverise it like the residues of other animal fluids, in order to submit to further analysis a newly dried and weighed quantity. The etherial extract contains fat, and not unfrequently also a little of the resinous biliary matters, which may be separated from the fat by aqueous spirit. The residue insoluble in ether, which contains the essential constituents of the bile, must be dissolved in absolute alcohol; we must then remove the greater part of the alcohol by distillation or evaporation, and treat the concentrated fluid with ether as long as any turbidity is observable; there then generally only remains a very little alkali in combination with a fatty acid, and some chloride of sodium in the ethereo-alcoholic fluid; the fluid with its precipitate must, however, stand for a considerable time in a cool place, because the alkaline glycocholate only separates very slowly. The salts of the biliary acids which are thus separated, are unfortunately always mixed with bile-pigment, from which they can only rarely be separated by the addition of chloride of calcium to their alcoholic solution (namely, when the pigment consists of true cholepyrrhin). By dissolving in alcohol a portion of the mixed glycocholates and taurocholates precipitated by ether, and by adding sulphuric acid to the solution, we can determine the quantity of the soda or potash in combination with these salts and with pigment, and we can ascertain whether or not ammonia be present. Unfortunately the determination of the alkali in this way is not strictly accurate, since a little chloride of sodium and soda in combination with a fatty acid, always occur in the precipitate thrown down by the ether, and thus contribute their alkali to that with which the biliary acids were combined. An exact separation of the taurocholic and glycocholic acids is impossible (as indeed is obvious, from what has been stated in vol. i. p. 232); consequently the best method of calculating the amount of the biliary acid yielding taurine, is by determining the quantity of sulphur in the biliary salts* which have been precipitated by ether; for this purpose we oxidise a weighed portion of them with potash or soda and nitre in the dry way, and determine the sulphuric acid that is formed. As, even if sulphates had been present, no sulphuric acid could have got into the alcoholic extract, it is obvious that all the sulphuric acid that is found, must have been derived from the sulphur which was in combination with organic matter; and taurocholic acid is the only sulphurous substance contained in the alcoholic extract.

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* [The alkaline taurocholates and glycocholates.—G. E. D.]

The residue of the bile insoluble in absolute alcohol must now be determined with the view of checking the analysis; it contains pigment, partly free and partly in combination with lime, alkaline and earthy phosphates, with a little alkaline carbonate and chloride of sodium, very rarely sulphate of potash, but often a little taurine; its amount is generally so small that any further quantitative determination, as, for instance, by means of diluted spirit, water, acids, &c., is hardly practicable.

Those who have studied all that has been stated in the first volume regarding these substances and their properties, need hardly be informed that the methods of analysing the bile can, and indeed must, be variously modified, and that the method we have just given can only serve the purpose of an illustrative scheme.

We have stated in the first volume all that is necessary regarding the quantitative determination of the cholesterin and fatty acids. These substances can only be determined quantitatively when a very large quantity of bile is submitted to analysis.

Biliary concretions must be ranked amongst the morbid products of the secretion of the liver. Few points in pathological chemistry, in the earlier period of that science, have received so much attention as gall-stones; but all the very numerous observations which have been made regarding them are reducible to the following facts: these concretions occur principally in the gall-bladder, more rarely in the biliary ducts; in women more frequently than in men, and especially in aged persons: they often co-exist with cancer of the liver or of other organs, but it cannot be positively affirmed that carcinoma is a predisposing cause of gall-stones, since both these adventitious products specially pertain to advanced age and to the female sex; each is, however, often found independently of the other. Gall-stones appear to be of more common occurrence in England, Hanover, and Hungary, than in other countries. Most gall-stones are so rich in cholesterin, that the other constituents are of very secondary importance; all, however, contain one or more nuclei, consisting of traces of mucus and earthy phosphates, but principally of an insoluble combination of lime with bile-pigment: a large number of gall-stones are formed of a mixture of *cholesterin* and *pigment-lime*;* the latter is sometimes uniformly distributed through the concretion, in other cases we observe alternating layers of choles-

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* [Pigmentkalk in the German; it is the compound noticed in page 65.—G. E. D.]

terin and the brown pigment, and in others again we find only a little cholesterin in the dark brown mass of pigment-lime.

There is a third kind of concretion which is comparatively rare, namely, the black or dark green variety; this contains another modification of the pigment, which however, in this case also is combined with lime: this variety is usually free from, or at all events very poor in cholesterin.

Biliary concretions, in which carbonate and phosphate of lime are the principal ingredients, are very rare. (Bailly and Henry, Steinberg.)

It is singular that *uric acid* has occasionally been found in gall-stones. (Stöckhard,* Marchand.†)

All gall-stones absorb a little bile, which may be readily abstracted from the pulverised concretion with water or cold alcohol.

The *forms* of gall-stones are extremely varied; while some are very regular and symmetrical, others assume the most unaccountable shapes.

Bramson ‡ has undoubtedly indicated an important point in relation to the formation of the majority of gall-stones—namely, that it depends on the separation of a compound of pigment with lime.

Although Bramson's view has been much contested, we can undoubtedly recognize the presence of a compound of pigment with lime in the residue of the nuclei both of cholesterin concretions and of the brown gall-stones after extraction with alcohol and water, although we are, as yet, unable to establish a definite proportion between the pigment and the base. Every residue which is rich in pigment always contains a greater or lesser quantity of earthy phosphates and a little mucus; these earthy phosphates most probably originate from the mucus, which, however, like the protein-bodies in the formation of phlebolites, gradually dissolves and disappears; for the phosphates never stand in a constant ratio to the mucus remaining in the concretion; the mucus may also contain a little lime, which on incineration is converted into carbonate and sulphate; moreover, we sometimes meet with oxalate of lime, although only in very small quantity; I have never found pre-formed carbonate of lime in the brown residue of gall-stones (if present, it may be very readily detected by observing, under the microscope, the effect produced by a little acid

* De Cholelithis diss. inaug. med. Lips. 1832.

† Journ. f. pr. Ch. Bd. 25, S. 39.

‡ Zeitschr. f. rat. Med. Bd. 4, S. 193-208.

on the substance previously moistened with water and freed from all air-bubbles). Sulphate of lime does not exist pre-formed, or at all events it is only present in very small quantity.

The ratio of the ash to the organic substance in the insoluble portion of gall-stones is altogether variable; in the insoluble part of six different concretions, there were 8·5, 12·1, 16·6, 30·4, 46·3, 50·6, and even 54·7% of ash; in the analyses of these six ashes there was comparatively much carbonate and little phosphate of lime according to the smallness of the ash; that is to say, in proportion as organic substance preponderated in the insoluble residue of a concretion, so much the more was the phosphate of lime encroached upon by the carbonate. In the ash which amounted to 8·5, there were 7·994 parts of carbonate of lime, and only 0·492 of earthy phosphates; while in the ash which amounted to 54·7, there were only 12·135 parts of carbonate of lime, a portion of which originated from oxalate of lime, which was recognised in the fresh object. Bramson has pointed out that dilute acetic acid extracts lime from the insoluble residue of biliary concretions; as this lime cannot be combined with sulphuric or oxalic acid, and as only an extremely minute quantity can be associated with phosphoric acid, it must be obtained from a combination with an organic substance: and as there is too little mucus present for us to ascribe it to that cause, it must necessarily have existed in combination with the pigment.

Further, if the bile-pigment were not in combination with some substance, it would be soluble in alcohol; for it is by no means a modified pigment which has become insoluble through some molecular change, but actual cholepyrrhin, in combination however with lime; and if we remove the lime by the application of a dilute acid, we obtain the cholepyrrhin, which is then soluble in alcohol, and possesses all the properties which we formerly enumerated.

An enormous deal has been written on the *formation* of the different varieties of biliary calculi, as well as regarding the proximate cause of the deposition of solid particles, and especially of the cholesterin; but any analyses of the various hypotheses that have been brought forward in relation to these points, would be here altogether out of place. The following is all that is actually known regarding the mode of formation of the concretions. Mucus and epithelium generally yield the points or foci around which a deposition of solid particles occurs; we always find pigment-lime with a little mucus in the centre of the concretion, and hence we may fairly conclude that it plays a part in their formation; but the separation of cholesterin from the bile is still not explained, even though mucus and pigment-lime can and must act as solid points. The question suggests itself, whether the bile lying amongst the gall-stones is normal in its character: it has been believed that it presents nothing abnormal,* but no conclusions can be drawn from any analyses of human bile that have yet been instituted, for the quantity of bile obtained from a dead body is too small to admit of an accurate analysis; moreover, the constitution of the bile when obtained after death, is generally more dependent on the morbid process which gave rise to the fatal termination, than on that which led to the formation of biliary concretions. It is, however, more than probable that in order that concretions of cholesterin should be formed, the bile should contain a smaller amount of the solvent for this substance than the normal fluid contains; but, as has been already mentioned, we very rarely meet with bile in which there is a separation of minute tablets of cholesterin, although they often occur in other fluids, as, for instance, dropsical effusions, &c.; hence the presence of solid insoluble particles must be regarded as exercising a considerable influence on the formation of gall-stones. If we inquire what it is which holds the cholesterin and the pigment-lime in solution in normal bile, direct experiments afford an answer to the question, and show that both these substances are principally held in solution by taurocholic acid or taurocholate of soda. If we digest the insoluble residue of a brown gall-stone with taurocholic acid or acid taurocholate of soda, it is entirely dissolved with the exception of a few greyish-white flocculi, and the previously colourless solution assumes the tint of fresh bile. Strecker showed long ago that cholesterin was soluble in solutions of taurocholic acid and its salts. Glycocholic and cholic (Strecker's cholalic) acids possess this property in a far less degree. The question regarding the formation of gall-stones would be very readily answered if it could be proved that bile which has a tendency to form concretions, was either poor in taurocholic acid in relation to cholesterin and pigment-lime, or that its taurocholic acid was decomposed in the gall-bladder and had thus lost its power of dissolving these two substances.

Since concretions, which are rich in cholesterin, are never entirely devoid of pigment-lime, while, on the other hand, calculi which are poor in cholesterin, are always very rich in pigment-lime, the idea suggests itself that this latter compound takes an

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* Novi comment. acad. scient. inst. Bononiens. T. 3, p. 307-317.

active part in the primary formation of these concretions; indeed, the frequency of their occurrence in certain districts in which the water abounds in calcareous salts, and in old age, (when, as is well known, there is an increased tendency to all kinds of calcareous deposits, and when the separation of cholesterin is promoted by the attenuation of the animal juices,) seems strongly to favour this view.

We at present possess very few results, upon which the slightest reliance can be placed, regarding the *quantity of the biliary secretion.* By proceeding on perfectly different assumptions, some physiologists have calculated the amount of bile secreted in the human subject in twenty-four hours, at only one ounce, while others have considered that it amounts to as much as twenty-four. Blondlot, from his observations on dogs, in which he had established fistulous openings into the gall-bladder, calculated that one of these animals secreted between 40 and 50 grammes of bile in twenty-four hours; and hence that the amount secreted by man during the same time, would be about 200 grammes [or between 6 and 7 ounces]. Bidder and Schmidt† have investigated this subject in a most accurate and ingenious manner. They arrive at the conclusion, from a large number of experiments on cats, that a cat weighing one kilogramme [nearly three pounds], when its digestion is most perfect, that is to say, when its biliary secretion is most abundant, secretes 0·765 of a gramme of fluid bile, corresponding to 0·050 of a gramme of solid residue in an hour; while, after ten days' fasting, there is secreted in the same interval only 0·094 of a gramme of fluid bile, yielding, when dried at 100°, a solid residue of 0·0076 of a gramme.

The secretion of bile is continuous; but, as is shown in the above cases, it is augmented or diminished according to the state of the digestion. Bidder and Schmidt found that the secretion attained its maximum ten or twelve hours after a copious meal, and from then till twenty-four hours after the meal, it gradually diminished, till it attained the same quantity which was secreted one or two hours after eating. In prolonged starvation, the quantity of the secreted bile gradually and progressively diminishes.

Thus, for instance, if a cat, weighing one kilogramme, discharges 0·492 of a gramme of fresh bile (obtained direct from the

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[*] I am indebted to the kindness of Dr. Schmidt for these results. The excellent memoir, containing a detailed account of their experiments, is not yet published. [It has since appeared, and is often referred to in the third volume of this work.—G. E. D.]

common biliary duct through an introduced canula) during the second hour after feeding, the quantity increases so rapidly, that during the fourth hour it secretes 0·629, during the sixth 0·750, the eighth 0·825, and in the tenth hour, 0·850 of a gramme of bile; so that, from the second up to the end of the tenth hour, the quantity of bile secreted increases, on an average, by 0·045 of a gramme in an hour. Moreover, the diminution in the secretion of bile takes place somewhat rapidly after the end of the tenth hour, the average hourly decrease from this maximum to the end of the twenty-fourth hour being 0·028 of a gramme.

With the view of determining the quantitative relation of the biliary secretion to the other animal excretions—a point of the greatest importance in estimating the physiological value of the bile—Bidder and Schmidt have instituted a series of statistico-analytical experiments on dogs, on about forty cats, thirteen geese, and several sheep and rabbits, in which biliary fistulæ had been instituted. They first determined the amount of carbonic acid expired by these animals, and then ascertained the ratio in which the secreted bile stood to it; and the result of these laborious investigations is, that "only from 1-10th to 1-40th of the carbon separated by the lungs is secreted in an equal time by the liver in the form of bile, so that at least 8-9ths or 9-10ths of the burned and expired combustible materials do *not* pass through the intermediate stage of bile, but remain in the circulating blood, where they become thoroughly oxidized."

In order to be enabled to form a definite opinion regarding that much disputed question, the physiological importance of the bile, it will be expedient previously to establish a view regarding the *origin* or formation of the bile, from the facts with which science has as yet supplied us. The biliary secretion has always been regarded either as a pure function of the digestive process, or as a definite factor in the general œconomy of the animal organism. The difficulty of deciding between these views seems half removed when we have a clear understanding regarding the formation of the bile, that is to say, regarding the substances from which its proximate constituents are formed. We have already seen in the first volume that unfortunately there is still considerable obscurity regarding the origin of the individual substances which constitute the bile. Nevertheless, we trust to find in certain positive experiments and observations, a logical justification for either one or the other hypothesis. That which applies to the individual constituents, applies also to the bile collectively; the following facts will, however, probably indicate the path by which we may arrive at a knowledge of the mode of origin of the bile. The first point in this investigation is, to decide the question where the formation of the biliary constituents actually takes place, that is to say, whether they exist ready formed in the blood, or whether they are first formed in the secreting organ. The larger number of well-confirmed facts tend to show that the principal constituents of the bile are primarily formed in the liver itself from certain constituents of the blood conveyed to this organ by the portal vein. On comparing the histological formation of the liver with that of the kidneys, we perceive that in the liver there cannot be a pure transudation—a mere process of filtration of certain constituents of the blood—such as occurs in the kidneys. We know that in the liver the most minute blood-vessels are separated from the smallest canals which convey the bile by a thick layer of tolerably large cells, and that consequently in every case the substances given off from the blood must pass through cells endowed with vital force, before they can enter into the biliary canals. No comparison can be instituted between these cells and the epithelial cells which occupy the ducts of Bellini; for these hepatic cells close the extremities of the biliary canals (whether these form blind and distended sacs or very minute loops); if the smallest biliary canals possess a *membrana propria,* these cells, united in rows and having a cœcal arrangement, lie external to it, and consequently in this respect differ essentially from the epithelial cells of the *canaliculi contorti* of the kidney, which take no part whatever in the urinary secretion. But the microscope which reveals to us the contents of these cells, indicates that they are elaborated from materials resorbed from the blood; for in addition to the round nucleus occurring in these cells, they contain a greater or less quantity of small molecules and vesicles, which very often become developed into distinct fat-globules; in numerous cases, however, these hepatic cells are filled with a yellowish matter, which sometimes appears in the form of distinct and separate molecular granules, and sometimes as diffused masses. With regard to the colourless fat-globules, they must necessarily undergo a metamorphosis within the cells, since very little free fat is generally found in the bile. From certain microscopical observations which I made in reference to the morphological contents of the hepatic cells of dogs and rabbits at different periods after taking food, it seems to follow that their physical characters vary with the stage of the digestive process. These and other histological relations which have been observed by Meckel[*] and Leidy,[†] show that it is, in these cells that the substances taken up from the blood are elaborated into bile; and most of the physiological facts with which we are at present acquainted, accord with this view. Müller, and subsequently to him, Kunde,[‡] after separating the skin of the abdomen and tying the portal vein, opened the abdominal cavity of large frogs; ligatures were applied to all the points of attachment of the liver, and that organ was completely extirpated; after the operation, the animals were kept in narrow, dry vessels, at a low temperature, and the blood of those that were still surviving after two or three days, was collected by amputating their thighs. As we are justified in concluding, both from the experiments of Blondlot and from pathological observations, that icterus ensues within two or three days after the occlusion of the gall-ducts, we must here expect to find a very large quantity of bile-pigment and cholic acid, if the formation of the most essential biliary constituents take place externally to the liver; but although the examination was conducted with the greatest care, we could not detect, with certainty, any trace of either of these substances in this blood.

I must here remark, that at the commencement of these experiments we believed that, though we could find no bile-pigment, we had detected biliary acids; but we subsequently convinced ourselves that frogs' fat, and indeed any fat that abounds in olein, yields with sugar and sulphuric acid a reaction extremely similar to that of cholic acid. But after we had become acquainted with this source of error, and had, as far as possible, removed the fat, no trace of bile could be recognised either by Pettenkofer's test or by any other means (as, for instance, the exhibition of taurine, the determination of sulphur in the alcoholic extract, &c.)

It certainly cannot be denied that after such severe operations, conclusions should only be drawn with the most extreme caution; but when taken in association with the above-named histological and with the physiological and pathological facts presently to be mentioned, the result to which we have been led by our experiments is deserving of a certain amount of weight.

It is further known that the biliary secretion differs from all other secretions in this respect, that it proceeds from the capillary system of a vein, and that even the blood of the hepatic arterial

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[*] Müller's Arch. 1846.

[†] American Journal of Medical Science. Jan. 1848.

[‡] Diss. inaug. Berol. 1850.

branches has become venous before it comes in contact with the finest ramifications of the biliary ducts; for, as Kiernan was the first to show, the *vasa vasorum* of the hepatic artery enter into a venous plexus which, instead of opening into the hepatic veins, discharges itself into the smaller (but not the smallest) branches of the portal vein, and in this manner forms the hepatic origin of the portal system. Hence the secretion of the materials of the bile takes place solely from pure venous blood. The secretion in the kidney, for instance, is altogether different, to which arterial blood, and with it the substances (such as urea, uric and hippuric acids, &c.,) which are first rendered excrementitious by the respired oxygen, are carried, and where, without having to pass through a dense layer of cells, these substances are transmitted in a manner very similar to simple transudation from the blood-vessels into the urinary canals. From the extreme slowness with which the blood passes through the liver, it follows that the conversion of the constituents of the blood into bile in the hepatic lobules only takes place very gradually, thus allowing of a more thorough and complete metamorphosis. (At these lobules, we find that the finest capillary network of the portal vein is separated by the plexus of the hepatic cells from the smallest biliary canals, which, according to E. H. Weber, are far more minute than the finest capillary vessels.) If we consider that the blood of the portal vein has been already collected from a capillary network, and that now, without further mechanical assistance, it has again to overcome the resistance of friction in a second capillary system, and further, that the veins into which the portal branches discharge themselves, are even deficient in the valves which usually aid the circulation within the veins, we can comprehend why it is that the blood passes very slowly through the liver. Müller and E. H. Weber have convinced themselves of the correctness of this assumption by direct microscopic observations on frogs and on the larvæ of salamanders. With these facts in our possession, we need be as little surprised that Bidder and Schmidt perceived that two hours elapsed after the administration of food, before there was an augmentation of the biliary secretion, and that it was not till the end of ten hours that the *maximum* flow took place, as at the great frequency of hyperæmic affections of the liver and of the associated congestion of the hæmorrhoidal veins.

If, however, the great slowness of the circulation within the liver forces us to the assumption that there is a peculiar elaboration of the materials in question within the hepatic cells, so also does the source of the substances which are conveyed into the portal blood, point to the peculiar function of the liver as a metamorphosing organ. The venous blood proceeding from the stomach, the whole intestinal canal, and from the mesentery, is collected in the portal vein; hence a great part of the nutrient matters absorbed in large quantity by the veins of these parts is conveyed into the liver; moreover the veins of the pancreas, and (what is more essential) those of the spleen, pour their blood into the portal vein. We shall presently see, when treating of the chemical and physical investigation of the blood, that the character of the portal blood varies according as the portal vein receives most of its blood from the stomach and intestinal canal during the process of digestion, or from the splenic veins, which convey a fluid very different from other venous blood. We shall, however, also see that the blood of the hepatic veins is as different from portal blood (whether collected during fasting or while the digestive process is going on) as from the blood of any other portion of the venous system. The blood within the liver, in its transition from the arterial into the venous state, undergoes more striking alterations than in any other organ. These changes are not confined to the mere abstraction of individual constituents from the blood in the liver, but, as we shall presently see, some of its constituents have undergone very distinct chemical changes. To this we must add, that the presence of the most important constituents of the bile cannot be recognised as pre-formed in the portal blood, notwithstanding many assertions to the contrary: at all events I have never succeeded in detecting them, even when operating on very large quantities.

The principal arguments against the view that the bile is formed from heterogeneous constituents within the liver itself, are based partly on the supposed analogy between the biliary and the renal secretions, and partly on certain pathological phenomena. That the analogy between the renal and hepatic secretions is limited to the single fact that they both are secretions, is sufficiently obvious from what is known regarding the difference in the structure of the two organs; and in reference to the facts derived from pathology, these, upon the whole, rather accord with the view that the bile is formed in the hepatic cells than that its actual constituents pre-exist in the blood. Jaundice very seldom occurs in diseases of the parenchyma of the liver, and almost never in the different forms of fatty degeneration or in tuberculosis of the liver, and very rarely in simple and red atrophy, in granular liver, and hepatitis; while the only diseases in which it is almost constantly present are those of the biliary ducts and acute yellow atrophy. If an accumulation of actual (chemically recognisable) biliary matters were induced in the blood by the suppression of the hepatic secretion, jaundice would necessarily occur just as frequently in the above-named diseases, which affect the parenchyma of the liver, as in impeded excretion of the bile. It is true that these diseases rarely attack the whole parenchymatous structure (indeed, hepatitis never does so, and jaundice seldom occurs in this affection), so that a portion of the liver could always provide for the separation of the bile from the blood: but again, on the other side, the facts may be urged that, in association with jaundice, there may be an abundant flow of bile into the intestine (as, for instance, may occur in pyæmia, yellow fever, after the bites of poisonous snakes, and even in cases of pneumonia accompanied by icterus), and especially that jaundice may occur in diseases in which no organic change either of the parenchyma or the gall-ducts can be detected. At all events this much is obvious, that we are unable to draw any conclusions from the presence of jaundice regarding a disturbance of the secretion of the liver or the separation of bile, and that it yields us no means of arriving at an opinion regarding the suppression of the biliary secretion or the formation of bile in the liver. Positive data are still required in order to enable us to decide, from the occurrence of jaundice, whether there is a mere separation or a secretion of bile; the different conditions which accompany or give rise to its occurrence are still so little investigated, that we are by no means justified in concluding that there is a formation of true bile in the blood, even in such cases as acute yellow atrophy of the liver (in which, in addition to the sudden access of jaundice, we find even the hepatic cells atrophied and destroyed).

In connexion with this subject we would merely direct attention to some few points which have hitherto not been sufficiently rearded, in reference to pathological conditions. Thus, for instance, it is still undecided whether other biliary matters, and more particularly the coagulated resinous acids, are found in the blood simultaneously with icterus; and it would even appear probable, from certain observations, that icterus may be present when no biliary acids are found in the blood. If it could have been shown which biliary acid,—that is to say, whether a conjugated acid or cholic (Strecker's cholalic) acid or choloidic acid—occurred in the blood of persons affected with icterus or in healthy individuals, it might have been determined whether its resorption was effected from the liver through the lymphatics or from the intestinal canal; but owing to the uncertainty of Pettenkofer's bile-test, our conclusions regarding the presence of the biliary resinous acids must be wholly subjective. The lymphatics undoubtedly play a highly important part in the resorption of the bile, and these vessels are moreover alone able to absorb bile from the liver, as the venous plexuses of the hepatic artery open into the portal vein, and would therefore convey the recently absorbed bile back to the hepatic cells. In the dead body the bile readily infiltrates into the neighbouring parts, but in living animals such is not the case; it is probable, however, that we might also observe a similar imbibition of bile during life if it were not directly absorbed by the lymphatics surrounding and intersecting the surface of the liver as well as the biliary ducts and the gall-bladder. It is believed that many substances undergo chemical changes in the lymphatics; but it is not known whether bile-pigment and the biliary acids are carried unchanged through the healthy lymphatic system, or whether they experience any alterations in it. We do not know, therefore, whether or not the lymphatics perform their function in those diseases in which icterus is present without any obvious organic changes in the liver, or where, in addition to the jaundice, a large quantity of bile passes into the intestine. It would appear from experiments of injecting filtered bile into the veins, that the blood possesses the property, when in a normal state, of exerting a metamorphic action on the biliary matters; yet life may be prolonged for years after the complete occlusion of the ductus choledochus. We are, however, ignorant whether the blood in febrile and inflammatory conditions—where its oxidation is considerably diminished —loses the capacity for metamorphosing these biliary matters like the extractive matters, uric acid, cystine, &c. Why does icterus occur in fatty liver only when acute diseases supervene? In granular liver many of the small biliary ducts may be obliterated, and the hepatic granules consequently filled with bile, and yet icterus may not have been manifested during life. Acute yellow atrophy of the liver is a disease that has been but seldom observed, and still less investigated (excepting by Rokitansky); of the chemical metamorphoses by which it is attended we know nothing. We do not think, therefore, that the meagre observations hitherto made by the bedside and in the dead-house justify us in drawing conclusions regarding the formation of bile in the blood, and the occurrence of icterus from the suppression of the biliary secretion.

If the view that the *formation of bile* takes place in the liver itself appears to derive considerable probability from anatomical and physiological facts, and is certainly not refuted by our pathological observations, we are necessarily induced to compare the juices conveyed to the liver with those flowing from it; since it is only by a comparison between the fluids entering and leaving the liver that we can hope to attain certain and fixed points of support for a chemical survey of the mode in which the bile is prepared from different organic elements, and thus avoid too wide a deviation from the truth. If it be admitted that the portal vein mainly supplies materials to the liver, we must seek in the blood of this vein for the substances which contribute towards the formation of bile; and when the advanced state of our chemical knowledge shall enable us to institute a comparison between the constitution of the blood of the portal vein and that of the hepatic veins, it will necessarily be the means of elucidating the mode of formation of the bile and the function of the liver.

Unfortunately, however, chemical analysis is not in a sufficiently advanced state to afford a satisfactory reply to all, or even to many of the questions which we hope to solve by its aid; but yet it affords us the means of confirming or refuting some of the arguments advanced in support of one or the other of the above views. As we purpose, in our remarks on "the blood," to enter more explicitly into the consideration of the different parallel analyses which we have made of the blood of the portal vein and of the hepatic veins, we will limit ourselves in the present place to a mere notice of the results in question.

The comparison between these two kinds of blood is probably more disturbed by deficiencies in our chemico-analytical appliances, than either by the admixture of blood originating from the hepatic artery with the blood of the hepatic veins, or by the abstraction of materials by the lymphatics. As far as concerns this addition of the blood of the hepatic arterial branches when it becomes venous, this is very small; for, independently of the small calibre of the hepatic artery, which is far less than that of the portal vein (a section of the hepatic artery is 4,909 square lines, while that of the portal vein measures 38,484 square lines, according to Krause and Valentin), the rapidity of the circulation of the blood in the veins proceeding from the hepatic artery must be nearly as small as in the equally large capillaries of the portal vein. The lymphatics, however, appear chiefly to absorb the material resulting from the nutrition of the vessels and the biliary ducts by the hepatic artery, and to carry off some portion of the previously formed biliary substances. On these grounds, it is necessary that a stringent comparison should be instituted between the blood of the veins which enter and leave the liver.

In passing to the consideration of the individual biliary substances, and inquiring which of these exist pre-formed in the blood of the portal vein, we find that none of the most essential constituents of the bile can be detected in it. The presence of resinous biliary acids, and therefore chiefly of cholic or choloidic acid, in the portal vein, has been conjectured even by those who do not believe in the formation of these acids in other parts than the liver; nor was their presence here to be wondered at, since there appeared to be grounds for assuming that a portion of the bile effused into the intestinal canal was resorbed by the veins, and that the rudiments of this resorbed bile must then of necessity be again collected in the portal vein; yet the most carefully conducted inquiries, instituted under various conditions, have hitherto failed to demonstrate the existence of these resinous biliary acids in the blood of the portal vein. The error of supposing that biliary substances have been demonstrated in the blood of the portal vein by means of sugar and sulphuric acid, arises from the similar reaction which Pettenkofer's test gives with olein and oleic acid.

We endeavoured in the first volume of the present work (see pp. 126 and 270) to demonstrate the chemical grounds on which we based our hypothesis that cholic acid must be regarded as a conjugated acid, consisting of a non-isolable modification of oleic acid and a carbo-hydrate. We were led to adopt this view mainly in consequence of the large quantity of olein contained in the blood of the portal vein, in which respect it differs so greatly from the blood of every other vein, including even the hepatic veins. A careful examination of the blood of the portal vein, and a comparison of this blood with that of the hepatic and other veins, lead almost involuntarily to the conclusion that the oleaginous fats which occur in preponderating quantity in the blood of the portal vein, and are only contained in very small quantity in the blood of the hepatic veins, must participate to a considerable extent in the formation of the bile; for the blood is rich in olein when it enters the liver, but exhibits only a very small portion when it leaves that organ; the fat of the blood of the hepatic veins is also more consistent, and contains relatively more margarin. On an average, the solid residue of the portal blood contain 3·225% of fat, while that of the hepatic venous blood contains only 1·885%.

I do not purpose reverting here to the chemical grounds which appear to support the view that cholic acid is formed from oleic acid, but would simply observe, in relation to this subject, that I have never succeeded in producing sebacic acid by dry distillation from cholic acid, and, on the other hand, that I have convinced myself that not only the acids of the butyric acid group (Redtenbacher), but likewise those of the succinic acid group, more especially lipic and suberic acids, may be produced from cholic acid by the action of nitric acid, in the same manner as from oleic acid (Laurent). Moreover, Kunde, as already observed, found that not merely the fat of frogs, but also every other animal or vegetable fat which is rich in olein, yields an intense purple-violet colour with sulphuric acid and sugar; it does not occur with fats that are free from olein, and is most perfectly exhibited with pure oleic acid. This reaction of the oleic acid only differs, according to my experience, from that of cholic acid in occurring more slowly, and requiring the access of atmospheric air. As I did not perceive that there was any absorption of gas, I thought that the oleic acid might be contained in the cholic acid, in the modification of elaidic acid; but the latter acid yielded the same reaction as cholic acid with sugar and sulphuric acid, although less rapidly.

M. S. Schultze* has recently made the same observation with regard to olein. He also showed that the protein-bodies yielded a similar violet colour when treated with sugar and sulphuric acid; and I have noticed the same circumstance in many ethereal oils, as, for instance, oil of turpentine and oil of caraway.† Pettenkofer's test is, however, by no means to be rejected on this account, as it merely requires the same amount of caution in its application that is indispensable for the exhibition of every other chemical reaction.

The fat of the hepatic venous blood, when treated with sugar and sulphuric acid, yields the same reaction as that of the portal blood; and, when the experiment is conducted with care, we can scarcely fail to arrive at the conviction that no bile is contained in either kind of blood. The reaction does not ensue excepting with that portion of these two kinds of blood which is soluble in ether,

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* Ann. d. Ch. u. Pharm. Bd. 71, S. 270.

† Kunde, De hepatis ranarum extirpatione diss. inaug. med. Berol. 1850.

and fails with those extractive bodies which are only soluble in alcohol—a fact which plainly indicates that these substances are not of a biliary nature.

The positive experiments, made under different physiological relations, by Bidder and C. Schmidt, on the biliary secretions of animals, appear, at first sight, to refute this hypothesis. These careful observers found that fat animals yield considerably less bile than lean ones, and that, when they were fed on fat (bacon, suet), the quantity was smaller than in the case of animals fed on substances containing the smallest possible portion of fat. These differences were no longer appreciable in animals which had been kept for some time without food. The fact that fat animals yield less bile than lean ones, is in harmony with an observation already referred to, that the metamorphosis of matter is usually accomplished more slowly, and in a smaller degree, in organisms disposed to secrete fat in abundance; we need only mention that fat animals expire less carbonic acid in equal periods of time than lean but strong ones. The inference to be drawn from these observations is, not that fat animals and fat persons yield little bile because they are fat, but rather that such animals and persons have grown fat in consequence of their secreting little bile.

It can scarcely excite surprise that animals which are fed exclusively on fat should secrete less bile; for all fat is not applied to the formation of bile, neither is it fat alone which is employed for that purpose; for we shall presently see that fat constitutes only a *part* of the material necessary for the formation of bile. Daily experience, derived from the pathological observation of cases of fatty liver, shows us also that an excess of fat is prejudicial to the secretion of bile, for, although the hepatic cells are often dilated to twice the normal size in these cases, the quantity of bile is very much below the normal standard.

Lastly, the circumstance that animals which are fasting secrete more bile than those which are fed exclusively on fat, does not refute this hypothesis; for, as *much* sugar arrests the progress of vinous fermentation, *much* fat also impedes the formation of bile in the hepatic cells. As far as we are able to observe the metamorphosis of tissue in animals which have been kept for a long time without food, it would seem that this change is not limited to those histological elements which contain nitrogen, for we find that the fat rapidly disappears during inanition. We have already spoken, in the first volume, of the possibility of the formation of fat from the protein-bodies. If the observations of the above-named distinguished experimentalists do not admit of the interpretation we have endeavoured to give to them, the circumstance that the quantity of fat entering the liver is greater than that which passes from it, must remain entirely unexplained.

Sugar, or, at all events, a carbo-hydrate, must be regarded as another element essential to the formation of bile. The chemical equation according to which cholic acid may be regarded as composed of oleic acid and sugar, would not possess a higher value than any other one that might very readily be established from the high atomic weight of cholic acid, were it not supported by other grounds. We mentioned in the first volume (see p. 290), that Bernard and Barreswil had found sugar in the tissue of the liver; and this discovery, which I have verified by my own observations, has been recently corroborated by the numerous experiments of Frerichs* on the livers of animals and men. This observer convinced himself that the quantity of sugar in the liver was wholly independent of the nature of the food—so far, at least, that it was discovered in the liver of animals which had been fed for a long time on flesh alone. We considered, at p. 292 of the first volume, the grounds which render it probable that sugar may be formed in the animal organism from the protein-bodies. Scherer† has recently drawn attention to a peculiar kind of sugar, incapable of fermentation, and found in the muscular juice; and C. Schmidt‡ believes that a small quantity of sugar exists in all normal blood. More or less sugar is always conveyed by the portal vein to the liver during the digestion of vegetable food; for we know, on the one hand, that the sugar which is gradually produced from starch through the whole course of the intestinal canal, is principally absorbed by the veins; and, on the other hand, that the veins of the stomach, and of the small as well as the large intestines, are emptied into the portal vein; and we consequently find, on a careful examination of the blood of the portal vein of the larger herbivorous animals, that it generally contains some portion of sugar, whilst this substance, as far as my experience goes, is much less constantly to be detected in the chyle. We are, therefore, disposed to agree with Frerichs in assuming that the sugar found in the parenchyma of the liver contributes, together with other constituents of the portal blood, at least in part, towards the formation of bile, although a large

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* Op. cit. p. 831.

† Verhandl. der physik. med. Gesellschaft in Würzburg. 1850. S. 51-55.

‡ Charakteristik der epid. Cholera. S. 162.

portion of the sugar formed in the liver is carried through the hepatic veins into the general mass of the blood. If our hypothesis of the constitution of cholic acid be correct, we can scarcely be surprised that sugar should lose 6 atoms of water in conjugating with oleic acid, when we bear in mind our previous experiences regarding conjugated compounds; but, after this union, we can no more detect sugar, as such, in cholic acid, than glycine in hippuric acid. (Compare vol. i. p. 190.)

C. Schmidt, although, as has been already mentioned, opposed to the view that bile is formed from fat, suggests the ingenious hypothesis, that in the metamorphosis of fat in the animal body, sugar and cholic (Strecker's cholalic) acid are formed from the neutral fats, that is to say, from the combinations of glycerine with fatty acids: it is certainly a fact of some interest that, when we assume that one-seventh of the hydrogen of the glycerine ($C_6 H_7 O_5$) is replaced by 1 equiv. of oxygen, we obtain the formula for anhydrous grape-sugar ($C_6 H_6 O_6$), and that when we take the fatty acid, $C_{48} H_{47} O_3$, (correspond to the general formula for the solid fatty acids, $C_n H_{n-1} O_3$,) and assume that 7 of its equivalents of hydrogen are replaced by oxygen, we obtain the formula for cholic acid, $C_{48} H_{39} O_9 . HO$.

In opposition to Bernard's "formation of sugar in the liver," C. Schmidt remarks that we find sugar in the blood of the vena cava, as well as in that of the portal vein; and in reference to this point I must observe, that I have found far more sugar in the blood of the hepatic veins (as noticed in the chapter on "the blood"), than in that of the portal vein or the jugular veins. In five determinations of these varieties of blood from different horses, I always found from 10 to 16 times more sugar in the solid residue of the serum of the hepatic venous blood, than in the corresponding residue from the portal blood; indeed, when the animals had been kept for some time without food, I could find no sugar in the portal blood, while it could easily be detected in the hepatic venous blood, and its quantity could be determined by fermentation. There can therefore be no doubt that sugar is formed in the metamorphoses which the blood undergoes in the liver. Now if we perceive an excess of fat and a deficiency of sugar enter the liver, and if we find that these substances emerge from that organ in an inverse proportion, it appears obvious and mathematically certain that, according to the above-mentioned hypothesis of Schmidt, the fat is decomposed in the liver into cholic acid and sugar. But although the above facts correspond so well with this hypothesis, we must consider that a formation of sugar may likewise be due to other substances. We shall presently see that there are also nitrogenous substances which undergo decomposition in the liver, and we have already (in the first volume) indicated the possible formation of sugar from such decompositions; and Scherer's discovery of inosite (muscle-sugar) renders this view still more probable. Finally, we at present know too little of the extractive matters, in which the portal blood is by no means poor, to feel justified in denying that some of them may be converted into sugar.

From all this it follows that, unless we would rest satisfied with mere chemical formulæ and equations, we are still very far from comprehending the individual stages of the metamorphosis of animal matter, and of recognising the nature of the changes that ensue, and the formation of the different new substances: the number of observations is, however, daily increasing, which must confine the admissibility and number of hypotheses within narrower and narrower limits. Thus, from the facts at present in our possession, we cannot decide with certainty which of the hypotheses regarding the formation of cholic acid — whether Schmidt's or the one I have propounded—approximates the nearer to the truth; probably neither presents a perfectly correct view of the actual case. The following circumstances seem to tell against Schmidt's hypothesis, and in favour of mine: unconjugated acids containing 9 atoms of oxygen, are, at all events, very rare in chemistry; oleic acid yields the ordinary reaction with Pettenkofer's test, which is not the case with the solid fatty acids (of the general formula $C_n\ H_{n-1}\ O_3$); and (which is of most importance) there is far less oily fat (although relatively more solid fat) in the hepatic venous blood than in that of the portal vein. This much only seems fully established from the experiments which have been described, that the liver is an organ in which sugar is formed.

We can very easily comprehend, and need hardly entertain a doubt, that the nitrogenous adjuncts of cholic acid (Strecker's cholalic acid) are formed from the regressive metamorphosis of the nitrogenous parts of the animal body, and therefore especially from the metamorphosis of tissue: but physiological chemistry should not merely indicate possibilities and probabilities in the animal processes, but it should, at all events for the future, teach us the chemical equations expressing the decompositions of the individual animal substances, and the manner and successive stages in which the metamorphoses occur. We are, certainly, still far from attaining this object, but it is time that we should endeavour to reach it by all the auxillaries and forces at our disposal.

Taking this view of the subject, it would be important to ascertain whether the adjunct which yields glycine or taurine, exists preformed (either free or in combination) in portal blood. In regard to the glycine, every attempt to detect it in portal blood has been unsuccessful, although as much as 450 grammes [about 15 ounces] was examined for this purpose; this experiment cannot, however, be definitely regarded as proving that no glycine occurs in portal blood, since the cause of the negative result may be dependent on the imperfection of our chemical analyses; but, at all events, the opposite view, in accordance with which the glycine of the cholic acid is first formed in the liver, is not overthrown by this experiment, and we shall presently point out the grounds which support the idea that the glycine is produced in the liver from the metamorphosis of nitrogenous matters. Moreover, we are equally unable to detect pre-formed taurine in portal blood.

According to F. C. Schmid,* the ash of portal blood is richer in sulphuric acid than that of blood from the jugular veins; we might be thus led to suppose that the sulphuric acid of the portal blood was applied in the liver to the formation of the sulphurous adjunct, but this is not the case. It is well known that the estimation of the sulphur in an ash-analysis is the most uncertain of any of the determinations in analytical chemistry, since it depends on various accessary circumstances (the mode of heating, the presence of carbon hard of combustion, or the absence of alkalies with which the sulphuric acid that is formed might combine), whether more or less sulphur is volatilised. In employing this inexact mode of determination, I was, however, unable to find the difference between the blood of the portal and the hepatic veins, which Schmid observed between that of the portal and jugular veins. The pre-formed sulphuric acid in the water-extract of the portal and hepatic venous blood appears to be variable; but as a general rule, I always obtained rather more sulphuric acid from the serum of hepatic venous blood than from that of portal blood: the augmented quantity in the first case is, however, only relative; for the serum of the portal vein, in becoming changed into that of the hepatic veins, not only loses much water, but also albumen, as we shall subsequently show. This much may, however, be regarded as certain, that the pre-formed sulphuric acid no more contributes to the formation of the sulphurous adjunct, than it passes into the bile. (See vol. i., p. 444).

If, however, we compare the quantity of sulphur in the two kinds of blood by the application of the dry method of oxidation,

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* Heller's Arch. Bd. 4, S. 323.

as, for instance, by potash and nitre, we find that the residue of the portal blood is certainly the richer in sulphur. On an average, I found 0·393 of sulphur (all the sulphuric acid being calculated as arising from sulphur) in 100 parts of the solid residue of portal blood, and 0·331 of sulphur in 100 parts of that of hepatic venous blood. The sulphur which is applied to the formation of this adjunct is therefore as latent (unoxidised) or combined in the portal blood, as in the adjunct itself. It now remains for us to enquire—to what substance does it owe its origin?

In the spirituous extract of portal blood (after the residue has been already extracted with ether and alcohol) I found a substance which, on incineration with nitre, yields sulphur. (As it can also be obtained when the blood has been previously neutralised, it cannot depend on any albuminate of soda that may have been dissolved by the spirit). Moreover this sulphur-compound is also found in lesser quality in the blood of the hepatic veins. It is possible that the taurine, which, as we know, is rich in sulphur, may be formed from this sulphurous extractive matter. The principal source of the sulphur of the bile, and especially of the taurine, might, however, be sought in the perfect disintegration of the fibrin in the liver. I shall show, when treating of "the blood," that the quantity of fibrin in hepatic venous blood is almost imperceptibly small, and, indeed, that often I could discover no fibrin whatever in it. The substance which was calculated as fibrin by Schultz and Simon, in their analyses of the blood of the hepatic veins, could not have really been that substance, but must have been the cell-walls of the blood-corpuscles, deprived of their contents by water. Hence, whether or not the extractive matters contribute to the formation of the nitrogenous and sulphurous adjuncts of the cholic acid, it is by no means improbable that the fibrin of the portal blood is applied in that manner. But there is reason to believe that these adjuncts are primarily formed in the liver, not merely from their absence in portal blood, but also on the following purely chemical ground: we have seen, in the first volume, that glycine and taurine are not to be regarded as existing pre-formed in glycocholic and taurocholic acids; it is, however, the ordinary rule (and only few exceptions are known to it), that the so-called conjugated compounds are not directly formed from the adjuncts into which they become separated on decomposition; chemical experience, therefore, renders it improbable that these conjugated acids should be formed from pre-existing taurine or glycine and cholic acid. Moreover, we can hardly expect that in the animal organism, where complex compounds are resolved into simpler ones (when the retrograde metamorphosis predominates), comparatively simple substances should unite to produce more complicated ones in the formation of excreted matters.

If we attribute to the fibrin which is decomposed in the liver a great share in the formation of the above-named adjuncts, we must also at the same time meet the objection which may be brought forward, that the fibrin may be applied to the formation of the young blood-corpuscles which are found in such large numbers in the hepatic veins. I have certainly never found the characters of portal fibrin to differ so much from that of other venous blood, in newly-killed animals, as has been observed by F. C. Schmid;* it appears, however, to be less contractile and less dense than that of other venous blood. This, at all events, appears not to be the form in which it can be applied to the construction of tissues or blood-corpuscles. Moreover, we see from a comparison of the portal serum with that of the hepatic veins, that the albumen in the latter is considerably diminished, and has probably been employed in the formation of blood-cells. According to my investigations, the albumen is to the other solid substances in portal serum as 100 : 12·5, while in the serum of hepatic venous blood (where, moreover, the salts are diminished by about 0·3) the ratio is as 100 : 27·4. Moreover, hepatic venous blood contains, both absolutely and relatively, far less serum than portal blood; when for instance, the intercellular fluid is to the moist blood-cells in the ratio of 100 to 150 (and this was the case when horses were killed five hours after feeding), the corresponding ratio in hepatic venous blood is as 100 : 330; or if (ten hours after feeding) the ratio in portal blood is as 100 : 35, the corresponding ratio in hepatic venous blood is as 100 : 138. Hence the portal blood, in its conversion into hepatic venous blood, loses a very considerable portion of its serum, while the latter parts with much of its albumen. The coagulable, soluble albumen of the portal blood has, therefore, in a great part passed over into the considerably augmented cruor which is formed by the blood of the hepatic veins. If it is not too bold an hypothesis to assume that this portion of the albumen is applied to the formation of the walls of the blood-corpuscles, this readily explains why the bile is so rich in sulphur; for, as we shall prove in a future page, the walls of the corpuscles of hepatic venous blood contain no sulphur.

Another important constituent of the bile is the *pigment*, which also cannot be detected pre-formed in the portal blood; and we have

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* Op. cit.

already shown (in vol. 1, p. 317) that, in all probability, it is formed from the blood-pigment; we shall, therefore, not again revert to the grounds on which this possibility or probability rests, but will merely observe that, if cholepyrrhin be actually a product of the metamorphosis of hæmatin, the process, at all events in the normal state, takes place in the liver. It appears no mere image of the fancy, to regard the distorted, speckled, irregular blood-corpuscles in the portal blood of fasting animals, as cells that are growing old; for, at all events, we find that the blood-cells leaving the liver by the hepatic veins, exhibit precisely those characters which we ascribe to young blood-cells; hence the cells of the portal blood do not undergo rejuvenescence in the liver, but suffer disintegration in that gland, and their remains are in part (the iron, for instance) applied to the formation of new blood-corpuscles, and in part are converted into excreted matters; hence it is very conceivable, that the hæmatin loses its iron and becomes converted into cholepyrrhin, which is mixed in the biliary canals with the other constituents of the bile. In instituting several comparative analyses with both kinds of blood, I found in 600 grammes of portal blood-cells, 0·384 of a gramme of metallic iron, and in the corresponding 760 grammes of blood-cells from the hepatic veins, 0·333 of a gramme of iron. Hence, however great may be the errors of observation, this much is certain, that the iron of the decaying blood-corpuscles of the portal vein is more than sufficient for the requirements of the young cells of the hepatic venous blood. If we regarded the view as tenable, that the quantity of iron in the blood-corpuscles, or in the hæmatin, has any influence on the colour, we would here notice the difference of tint presented by the blood of the portal and of the hepatic veins. F. C. Schmid has directed attention to the dark brown, sometimes velvet-like black colour of the clot of portal blood; the corpuscles of the blood of the hepatic veins always appear of an intense purplish violet colour, when seen in thin layers—a colour which I have never observed in portal blood, nor to the same degree in any other venous blood. Whether this deficiency of iron in the blood of the hepatic veins be simply dependent on errors of observation, or whether the missing iron must be regarded as having passed into the bile, are points which I will not venture to decide, although I have made three experiments which coincided very well with one another. Since, however, iron has been so often found in the bile, the difference in the numerical results is probably dependent on the nature of the changes going on in the liver, and hence a part of the iron conveyed by the portal vein is carried off through the liver into the intestinal canal. Moreover, I was unable to find any iron in the serum of the blood of the portal vein, when free from red blood-cells.

Of the remaining organic constituents of the bile, the *cholesterin* is that which has received the most attention. It occurs, as we have already seen, in normal blood (see vol. i. p. 278); and it is contained in that of the portal vein, although, in consequence of the preponderance of true fat, it can only be recognised and measured by the microscope with much difficulty. But independently of this, the frequent occurrence of cholesterin in morbid products (namely, in serous, encysted exudations, as, for instance, hydrocele) without any simultaneous affection of the liver, or without the simultaneous occurrence of other biliary constituents in the collective juices, sufficiently indicates that this substance is a product of the general metamorphosis of tissue, and that the liver is merely the organ by which, in the normal condition, this lipoid is separated.

We have already seen why the occurrence of gall-stones rich in cholesterin, will not warrant the conclusion that there is an increased formation of this substance. The separation of cholesterin from the bile depends only on mechanical causes, and is independent of quantitative relations. Were we inclined to assume that there was a cholesterin-diathesis, we should at all events be astonished to observe, that when we found an exudation consisting almost entirely of a pulpy mass of pure crystals of cholesterin, gall-stones were never, or very rarely, simultaneously present.

It is unnecessary to offer any remarks regarding the origin of the *fats* and the fatty acids of the bile, since we have so often referred to the abundance with which fat occurs both in the blood of the portal vein and in the hepatic cells; the saponification of the free fats proceeds also in other places; as, however, the fatty matters of the bile are for the most part saponified, while it is chiefly unsaponified fats which are found in the fat-cells, it would seem as if the fatty acids of the bile were first formed in the hepatic cells.

This circumstance appears to us to be opposed to the dehiscence of the hepatic cells assumed by certain authors; for even in fatty liver, or in certain physiological conditions in which the hepatic cells are filled with fat-globules, we neither find that the bile contains a large amount of unsaponified fat or any augmentation of the saponified fat, which must have been the case if the hepatic cells burst and discharged their contents.

In connexion with the *mineral substances* of the bile, we shall first notice the *alkali* which it contains, and which is combined with the conjugated biliary acids, with fatty acids, and with pigment. Since both the water-extract and the spirit-extract of the portal blood yield alkaline carbonates on incineration, we can easily comprehend the source of these alkalies. Moreover, the albuminate of soda, in its transmission into the blood-cells, must also lose soda, which may contribute to the saponification of the fats and the formation of the biliary acid. In examining the ashes of the blood-serum of the hepatic and portal veins, I have found about as much, and, indeed, often rather more alkaline carbonates in the former than in the latter; but it must be considered that the blood of the hepatic veins contains little more than half as much intercellular fluid as the portal blood, and that consequently the whole of the blood of the hepatic veins contains far less alkali in combination with organic matters, than the whole of the portal blood. The same relation holds also with the alkaline carbonates, which I have found to exist pre-formed (by the method described in vol. i. p. 438) in both kinds of blood: to determine them quantitively was impossible; but it appeared to me (and to several eye-witnesses, the experiments being frequently repeated) as if the portal blood, when placed under the receiver of the air-pump, began to evolve air-bubbles in a less rarified atmosphere, and more abundantly, than the blood of the hepatic veins.

The quantity of the soluble *phosphates* in the bile is extremely small; like the earthy phosphates, they principally arise from the mucus of the gall-ducts. I have not found a constant difference between the amount of soluble phosphates in the blood entering into and flowing from the liver; the earthy phosphates would rather appear to pass from the blood into the bile; at all events, I invariably found more earthy phosphates in the clot of portal blood than in that yielded by the blood of the hepatic veins.

With regard to the *alkaline chlorides* which abound in the ashes of bile, the different quantities occurring in the two kinds of blood sufficiently explain their origin; in the serum of the portal blood, which has a comparatively low specific gravity, we find from 0·28 to 0·31% of chlorine, while in the denser serum of the blood from the hepatic veins only about 0·22% is found. On the other hand, the amount of chlorine in the blood-cells is much the same in both kinds of blood, and averages about 0·165%. Hence a portion of the alkaline chlorides must pass from the serum of the portal blood into the growing or young cells of the blood of the hepatic veins.

The singular result at which Bensch and Strecker have arrived, namely, that the bile of the herbivorous mammalia contains almost only soda-salts, while the food of these animals is rich in potash and deficient in soda, may probably be explained in the following manner: potash-salts are abundantly separated by other organs of the herbivora, as, for instance, by the kidneys; but in the liver no such separation takes place, because the potash conveyed into it with the portal blood is used for the formation of the blood-corpuscles (for, as C. Schmidt was the first to show, the blood-cells are especially rich in potash); we have, however, just seen that a great part of the alkaline chlorides passes into the cells of the blood in the hepatic veins.

Lastly, I must not omit to mention that the blood of the hepatic veins always contains considerably less water than that of the portal vein, and that even after abundant drinking, the quantity of water in the blood of the hepatic veins is only very slightly augmented, while in the portal blood it is increased to an extraordinary degree. Hence it follows that this excess of water in the portal blood is effused in the liver into the biliary canals, and that the density of the secreted bile must be liable to extreme variation from the external physiological causes.

In horses that had not drunk much for five hours after feeding, there were from 70 to 110 parts more of water in the portal blood than in the blood of the hepatic veins, the standard of comparison being 100 parts of solid residue. However, in the latter case, the blood of the hepatic veins was the more aqueous of the two.

It is possible that this mode of explaining the origin of the individual biliary constituents may be set aside by further experiments, but notwithstanding its obvious imperfections, we have ventured to bring it forward, seeing that the principal object of an hypothesis is, in our opinion, to stimulate other inquirers to fresh investigations.

The following may be regarded as a brief abstract of the above view regarding the origin of the bile: while the non-nitrogenous and nitrogenous matters conveyed by the portal vein—most of which, even when in the blood, bear the character of substances in the process of metamorphosis—are applied to the formation of the biliary constituents, substances also pass into the bile, which must be regarded as the residua or secondary products of the process which gives rise to the formation or rejuvenescence of blood-cells in the liver; in the latter class we must especially place the fats and certain of the mineral constituents, while the nitrogenous substances, fibrin and hæmatin, are the most important members of the former. Hence we do not regard the bile as the product of the metamorphosis of any single morphological or chemical constituent of the animal body (neither of the fat-cells nor of the albuminates); but we believe that several substances, chemically and morphologically distinct from one another, undergo alterations in the liver, and that their individual products unite in the nascent state, and thus form the compounds and admixture of substances which we find in the bile.

In order that we may not omit any element which may contribute to our knowledge of the functions of the bile, we must still consider what finally becomes of this secretion in the intestinal canal; as, however, this subject will be discussed in the chapter on "the intestinal juice," it will suffice here if we merely communicate the result of our experiments. The bile becomes gradually decomposed in the course of the intestinal canal, the conjugated acids breaking up and forming choloidic (or cholic) acid, which become converted into dyslysin—a substance that may be traced even into the rectum and the fæces; although the amount of biliary residue of this kind diminishes in the lower portion of the intestinal canal to such a degree that we are almost compelled to adopt Liebig's view, according to which the resinous constituents of the bile are for the most part resorbed from the intestine into the vascular system. Notwithstanding that the intestinal veins opening into the portal system, and the lacteals, afford the only means by which these biliary matters might again enter the blood, I have never succeeded in detecting the presence of such substances either in the chyle or (as has been already mentioned) in the portal blood in the normal state during the process of digestion. Hence, if there is no fallacy regarding the small quantity of dyslysin found in the solid excrements, we should be compelled to assume that the already modified biliary matters, absorbed by the lymphatics, were so changed in the glands that they no longer admitted of detection by the chemical means at present at our command.

The bile-pigments, although very much modified, are also found in the solid excrements, in addition to cholesterin and taurine. The soluble mineral constituents of the bile return from the intestine into the mass of the juices, as was long ago shown by Liebig.

After the above facts, and the conclusions based upon them, we need only say a few words in order to arrive at a judgment regarding the numerous, and often opposite, views in reference to the *functions of the bile.* We will, however, first briefly notice the opinions which we have already laid down regarding the physiological value of this secretion. Formerly, the point chiefly contested was, regarding the *excrementitious* or *non-excrementitious* nature of the biliary secretion, while all agreed pretty well in considering that the function of the liver was to purify the blood by separating the bile from it. We have endeavoured to show, in a former part of this work (see vol. i. p. 26), that a separation of zoo-chemical substances into secretions and excretions is both inexpedient and illogical, and it is therefore unnecessary to enter into any further discussion on this point. The view that the secretion of the bile is for the purpose of purifying the blood, needs no special refutation, since it is devoid of any logical justification; for such metaphorical indications of imaginary processes, and such vague analogies, are expunged from the physiological enquiries of the present day. For the benefit of those, however, who are unable to give up the old view, and who still regard the bile merely as an effete carbonaceous matter which the respiration does not remove, it may be mentioned that the bile—a secretion also not poor in nitrogen and hydrogen—is not separated in any increased quantity when the process of oxidation in the lungs happens to be disturbed; that there are no pathologico-anatomical facts which favour the view that the liver can act vicariously for the lungs; and, lastly, that the separation of carbon by the liver, as compared with that by the lungs, is so trifling (as is shown by the researches of Bidder and Schmidt, noticed in p. 79), that the liver can hardly be regarded as essentially a blood-purifying organ, in so far as the elimination of carbon is concerned.

With regard to the *importance of the bile in the process of digestion,* and especially in chylification, it need hardly be observed that very different views have been advanced respecting the manner in which the bile acts upon the substances passing from the stomach into the duodenum. The oldest view is that which was advocated by Boerhaave, and originated by Sylvius de la Boe, according to which the bile contributes its alkali to saturate the acids of the chyme; and it does not appear to us to be open to so many objections as we usually find brought against it. It is certainly quite true that the bile can directly contribute littleor nothing to the neutralisation of the free acid; on the one hand, because the smallest quantity of acid added to the bile at once renders it acid; and on the other, because we find the chyme in the intestine still acid after the bile has been well mixed with it. The following appears to be what actually takes place: the alkali of the bile, occurring in combination with the resinous and fatty acids, must unite with the stronger acids of the chyme—namely, hydrochloric, lactic, and butyric acid,—and the resinous biliary acids which are thus liberated communicate an acid reaction to the chyme (as may be perceived by the application of litmus paper), until they are decomposed into dyslysin, or the insoluble resinous acids deprived of their adjuncts. Hence, in one point of view, the bile certainly contributes to the neutralisation of the free acids contained in the chyme. This subject will be more fully considered in the chapter on "the intestinal contents."

There is likewise another view regarding the uses of the bile in the intestine, which hardly deserves to be totally rejected. Haller was the first who ascribed to the bile the property of *dissolving fat;* the bile, however, only possesses this property in a slight degree, although one of it constituents, the taurocholate of soda, certainly has this power, as has been shown by Strecker. The bile, in consequence of its viscidity, undoubtedly promotes the disintegration of the fat into minute molecules; but, even in this respect, it is exceeded by other fluids. Hence we might believe with Frerichs, that the bile, at all events in association with the pancreatic juice, contributes to the perfect disintegration of the fat, and thus considerably promotes its absorption; and the results of several of the earlier experimenters, who, after tying the ductus choledochus, found an almost limpid, instead of a milky (fatty) chyle, would support this view. On the other hand, Bidder and Schmidt, in their experiments (which will be subsequently described), could observe no difference in the injection of the lacteals and the opacity of the chyle of animals to whom fat had been given, whether the bile was allowed to enter, or whether it was excluded from the intestine.

Some writers (and especially Hünefeld*) have ascribed to the bile a great *power of dissolving the chyme,* but neither starch, nor coagulated protein-bodies, nor any other of the constituents of the chyme, are essentially changed, even when digested for a long time with fresh bile; indeed, as a general rule, no change seems to be

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* Chemie u. Medecin. S. 105.

effected in these substances till the putrefactive process is set up by the biliary mucus. On the other hand, the water effused with the bile must not be disregarded as a solvent for the soluble portions of the chyme; we have already seen that the blood of the hepatic veins is always much poorer in water than that of the portal vein, and that the latter fluid often contains an extraordinary quantity of water; this water must necessarily often circulate from the intestinal veins into the portal vein, and from it, through the biliary ducts, back into the intestine, and must thus the more contribute to the gradual separation and extraction of the chyme, in consequence of its again losing in the intestine the substances it had taken up from the liver, owing to the insolubility of the biliary acids. This water is therefore differently freighted, according as it flows from the liver to the intestine, or from the intestine to the liver; or, so to speak, it percolates two different filters, each of which is only permeable for certain substances.

Moreover, it has been attempted to show that the bile exerts a general chemical action on the contents of the intestine, but these enquiries have led to directly opposite views. Some have considered that the bile exerts an *antiseptic* action on those constituents of the intestinal canal which have a tendency to decomposition; while others, again, ascribe to the bile the property of imparting *a definite direction to the metamorphosis* of these substances by its own decomposition. To those who would rest satisfied with such general views of the subject, we may observe, that the first of these opinions is, at all events, untenable; pure bile may certainly exert an antiseptic action on substances which become readily decomposed, as flesh, &c.; the bile, however, which is effused into the intestinal canal is not pure, but is mixed with mucus, which very readily undergoes decomposition, and, in point of fact, is actually decomposed in the intestine, as may be seen by the simplest observation. Hence we might, perhaps, be supposed to concur in the second view, according to which a definite character is impressed upon the metamorphosis of the food by the bile as a special ferment. But it must be frankly confessed that the assumption of *fermentative actions* in any process is nothing more than an indication of our positive ignorance. We shall, therefore, now proceed to the more special investigation of the metamorphoses which the individual constituents of the chyme undergo in consequence of the action of the bile.

We must by no means overlook the circumstance that the intestinal contents, when no bile is mixed with them, very soon undergo putrefactive decomposition; at all events, it has been found (by Frerichs) that, after tying the ductus choledochus, the contents of the intestines of animals thus operated on became completely putrid; and the same thing has sometimes been observed in patients with jaundice. In these cases Frerichs found in the bowels the substance yielding a rose-red colour with nitric acid, which was discovered by Bopp amongst the putrefactive products of albuminous bodies. No great weight, should, however, be attached to this circumstance, in so far as the digestive process is concerned, since (as has been shown in the experiments of Schwann and Blondlot) animals in whom the ductus choledochus was tied, and whose bile escaped externally by an artificial fistula, lived and discharged normal excrements for months.

The view brought forward by H. Meckel, that bile converts sugar into fat, has been refuted by several experimenters, and is no longer supported even by Meckel himself.

He digested bile with sugar, and after the digestion he found more ether-extract in the bile than in bile not digested with sugar. The cause of the error may be easily perceived: ether-extract is not fat; the metamorphosis of the bile with its mucus is promoted by sugar, for the non-nitrogenous resinous acids (which are not insoluble in ether) are then formed more rapidly and in larger quantity than when sugar has not been added.

Prout is of opinion that the digested protein-bodies are converted by the bile into coagulable albumen, and Scherer* has made an ingenious experiment by which he thinks he has confirmed this view; lastly, Frerichs† has repeatedly seen filtered chyle become coagulable on the addition of bile and the application of heat. These experiments, although not the slightest doubt can be cast upon their accuracy, cannot be quite convincing, since it is, at all events, objectively difficult to prove that, on the one hand, the whole of the albumen which already existed, and was only prevented from coagulating, was previously removed from the chyme, and that, on the other hand, the turbidity of the mixed fluid was not dependent on the decompositions and reactions of individual substances, but on true coagulation of albumen by heat or of casein by acetic acid. I treated the purest peptones of albumen, fibrin, and casein which I could prepare, with bile and other reagents, but failed in obtaining a substance coagulable by heat or acetic acid, although I modified the experiment in numerous ways.

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* Ann. d. Ch. u. Pharm. Bd. 40, S. 9.

† Op. cit., p. 836.

Frerichs himself attaches no great value to this reproduction of albumen by the bile, for he remarks that only the smaller part of the ingesta dissolved by the gastric juice finds its way into the intestinal canal; by far the greater quantity passing directly from the stomach into the blood, and consequently being not at all exposed to the action of the bile.

Scherer introduced a mixture of bile and of flesh which had been dissolved in gastric juice into a portion of washed small intestine, and after tying both its ends, suspended it for some time in distilled water at a high temperature; he then found coagulable albumen in the water surrounding the intestine. As Valentin suggests, it is possible that in this case a little albumen might be extracted from the vessels and glandules of the gut, even though it had been well wasted with water.

Moreover the experiments made on animals in which fistulous openings were established between the gall-bladder and the external abdominal walls (by which means all the bile that was secreted escaped externally), which have led Schwann,* Blondlot,† H. Nasse,‡ and Bidder and Schmidt§ to very opposite views, do not prove that the bile exerts any *very* great influence on the digestive process. If animals can live for two or three months, or even half a year, without the passage of bile into the intestinal canal, the function of this fluid in digestion must at all events be a very limited and probably only an indirect one, and this is the conclusion we should draw from the accurate and ingeniously devised experiments of Bidder and Schmidt; for, as has been already mentioned, the secretion of bile does not attain its maximum till the tenth hour after food has been taken, and by this time by far the greatest part of the ingesta has passed along the duodenum; hence the bile enters the small intestine at much too late a period to exert in it any great influence on the metamorphosis of the chyme. The biliary secretion unquestionably stands in a definite relation to digestion; a relation, however, which must be considered rather in the light of an effect or consequence of the digestive process than as an intermediate link in the process itself.

We are thus led back to the view to which we have often alluded, according to which the most important function of the liver is the *formation*, or at all events the *rejuvenescence of the blood-corpus-*

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* Müller's Arch. 1844. S. 127.

† Essai sur les fonctions du foie et de ses annexes. Paris, 1846.

‡ Handwörterbuch der Physiologie. Bd. 3, S. 837.

§ In a Private Communication.

cles, a view which, as is well known, was long ago rendered more than probable by E. H. Weber, and more recently by Kölliker, by numerous histological investigations of fœtal livers and of fœtal blood, as well as of the livers of tadpoles. Although we shall enter more minutely in another place, when treating of "the blood," into the consideration of the different views that have been promulgated regarding the origin of the blood-corpuscles and the different situations in which they may be formed, yet as the subjects are so closely allied, it may be expedient here briefly to mention the grounds in favour of the above view. Since the consideration that the liver is a permanent factory for blood-cells appears, even to us, to be somewhat paradoxical for many physiological reasons, we shall allow the facts which present themselves as the immediate results of our comparative analyses of the blood of the portal and the hepatic veins, to speak simply for themselves.

The blood of the hepatic veins contains a far larger number of *colourless blood-cells* (the so-called lymph-corpuscles) than the blood of the portal vein. They do, however, also occur in the latter, although very scattered, in twos or threes at different points, and they are of nearly equal size, very coarsely granular, and on the addition of acetic acid exhibit a bipartite or tripartite nucleus. In the blood of the hepatic veins they present a very different relation: on an average calculation, their number is at least fivefold that of the colourless cells in the portal vein; they present extreme differences in size, varying from 1-306th to 1-180th of a line; they have for the most part a very faintly defined outline, are slightly granular, and often resemble colourless yolk-cells; the smaller ones are usually somewhat more clearly defined, and exhibit dots on their surface; the larger ones become much swollen in water, but at a certain degree of attenuation appear to collapse; they then form dark and very prominent granular masses under the capsules of the coloured blood-corpuscles; the larger colourless cells swell very much on the addition of acetic acid, and then exhibit a *single,* large, lenticular, excentric nucleus. Moreover, these colourless cells, which are of the most varied sizes, are aggregated in groups of five, six, or seven.

As we must return to the fuller consideration of the colourless cells, when we treat of "the blood," and shall then, moreover, explain the reasons in support of the view that the red blood-cells are formed from the colourless ones, it will be sufficient simply to mention my own observations regarding these cells, in order to support, from this point of view, the claims of the liver as a blood-forming organ.

The *red cells* of the blood of the hepatic veins are altogether different from those of the portal blood; in regard to their grouping, I very often found them assume the nummular arrangement in portal blood (in horses five hours after they had taken food), while in the blood of the hepatic veins I could never find a trace of any such arrangement, but saw them lying together in irregular heaps; we have become acquainted, through the admirable investigations of F. C. Schmid, with the peculiar *colour*, the spotted appearance, and the irregular *forms* of the coloured cells of portal blood; nothing of the kind was ever discovered in the corresponding blood-cells of the hepatic veins; they presented a sharp outline, and a very slight, although a recognisable, central depression.

The *capsules* of the coloured cells in the two kinds of blood present well-marked chemical differences, especially in their relation to water. The coloured cells of ordinary blood, if watched under the microscope, almost entirely disappear when much water is added; this is also the case in portal blood, although here also, as in every other kind of blood, a few of the coloured blood-cells, or rather of their capsules, still remain visible. In the blood of the hepatic veins a very different state of things is, however, observed; on diluting it with from 30 to 50 times its volume of water, the blood-corpuscles certainly are changed, that is to say, they become pale, swell up, lose their pigment, and unite so as to form membranes which, under the microscope, resemble detached serpent's scales. We have previously observed, that these decolorized blood-cells in the blood of the hepatic veins, were formerly mistaken for fibrin; but we may readily convince ourselves by the microscope of the almost entire absence of fibrin in the cruor of hepatic venous blood, and by the following experiment, of the accuracy of this view, and of the great number of these indestructible corpuscles in the blood of the hepatic veins. On mixing the fluid expressed from the clot with 20 times its quantity of water, portal blood, like that from any other vein, yields a slight flocculent deposit, in which shreds of conglomerated cell-walls may be recognised by the microscope; if, on the other hand, we treat an equal volume of fluid strained from the cruor of hepatic venous blood with 20 times its quantity of water, there will be a flocculent precipitate of 6 or 8 times the bulk of the precipitate in the other experiment, (although the non-fibrinous cruor of the hepatic venous blood contains in its interstices one-half more serum than an equal volume of any other blood;) in this manner I obtained, after the most careful washing and boiling with alcohol, 0·245% of these cell-membranes from the clot of the portal blood, while from the hepatic venous blood, similarly treated, I obtained from 1·98 to 2·43%. This cell-membrane was perfectly insoluble in a solution of nitrate of potash (even after 48 hours' digestion at 35°); I was unable to discover sulphur in it by boiling it in potash-ley, &c.

If this behaviour of the membranes of the coloured cells of the hepatic venous blood indicates that there is here an excess of newly-formed or rejuvenescent blood-corpuscles, the proof that a formation of new blood-cells takes place in the liver is fully confirmed by a comparison of the *contents* of the corpuscles of the two kinds of blood. We find far less hæmatin in the cells of hepatic venous blood, than in those of portal blood; for on an average, 180 grammes of the moist cells of hepatic venous blood contain scarcely so much iron as 100 grammes of the cells of portal blood. On the other hand, there is more globulin or coagulable matter generally, and more chloride of potassium, but considerably less fat, in the cells of the hepatic venous blood, than in those of the portal blood.

In the blood of the hepatic veins, the *fibrin* is either entirely absent, or is present in mere traces; while in the portal blood, taken at the same time, we often find a perfectly normal, strongly contracting fibrin.

The *serum* is relatively much less abundant in the blood of the hepatic veins than in that of the portal vein; while in the latter there are 70 parts of serum to 100 of corpuscles, in the former there are only 32 parts of serum to a corresponding quantity of cells; if the portal blood happen to be rich in water, as, for instance, when there are 287 parts of serum to 100 of cells, the blood of the hepatic veins will, even then, not contain more than 73 parts of serum to 100 of cells.

The serum of the hepatic veins is certainly more concentrated than that of the portal vein; if we accurately compare the two, we find in the former, a relative and absolute *diminution of the albumen* (there being in 1000 parts of the serum of the hepatic venous blood fully a third less albumen than in an equal quantity of the serum of portal blood), while on the other hand, as has been already mentioned, the globulin in the blood-cells is relatively and absolutely increased. The *phosphates*, *chlorides* and *potash-salts* are diminished in the serum, but are in excess in the cells of the hepatic venous blood. *Sugar* is relatively and absolutely more abundant in the serum of the hepatic venous blood, than in that of the portal blood.

If from these facts we should regard the liver as a seat of formation of blood-corpuscles, in which certain residua of this process are at the same time perfectly eliminated from the blood, and appear in the form of bile in the excretory ducts of this gland, the above-mentioned observations of Bidder and Schmidt would no longer excite our worder. We can easily understand why the biliary secretion does not attain its height until ten hours after the ingestion of food, when we recollect the extreme slowness with which the blood circulates in the hepatic capillaries, and when we consider that the formation or rejuvenescence of the blood-cells would certainly require some time in order that they may attain the perfection they possess when leaving the liver by the hepatic veins, and that the secondary products (the biliary matters) naturally cannot be duly separated till this principal process is almost concluded. Hence it need no longer excite our wonder, that during fœtal life the liver should possess so relatively large a volume, that the blood of the fœtus is far richer in corpuscles than that of adults (Poggiale*), and that even during this period bile is poured into the duodenum, although there is nothing in the intestine to be digested. Assuming this view to be correct, we may further easily understand why, in hepatic affections, and especially when they arise in consequence of metallic poisons (which, as is well known, are most prone to localise themselves in the liver), the number of cells in the blood frequently appears to be considerably diminished.

If the bile is merely a secondary product of the formation of blood-cells in the liver, we need not wonder that the animals in Schwann's and Blondlot's experiments could live for so long a time without any considerable disturbance of the digestive organs or of the general health; and if these animals finally died when the bile was completely excluded from the intestine, their deaths might result from unobserved or unsuspected causes, such, for instance, as their licking up the bile, and thus disturbing the gastric digestion: but several of the above-mentioned circumstances show that the bile likewise discharges certain functions in the intestine, which without it are not so rapidly or so perfectly performed; thus, for instance, it promotes the finer disintegration of the fat contained in the food, hinders the chyme from undergoing putrid decomposition, purifies it, and saturates the stronger acids which

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* Compt. rend. T. 25, p. 198-201.

have passed from the stomach into the intestine. Although any one of these influences, taken alone, would not be of sufficient importance to affect the vitality of the organism, yet when long continued and collectively, they may excite such disturbances in the animal economy as gradually to destroy life. Hence if the absence of bile in the intestine does not exert a direct disturbing influence on the vital processes, it may indirectly lead to the destruction of the organism, just as we see disturbances induced in the circulation from very trifling mechanical deficiencies of the valves, which indirectly, and perhaps after many years, give rise to fatal results.

Lastly, we have to mention a ground comparatively unimportant in itself, which is opposed to the excrementitious nature of the bile, and in part explains the injurious effects which gradually ensue when the secretion is altogether excluded from the intestine; we refer to the resorption of certain constituents of the bile—a circumstance which has been very prominently put forward by Liebig. It has been already mentioned that we are unable to detect any traces of resorbed bile either in the chyle or in the portal blood, but that a careful examination of the contents of the bowel, in various portions of the whole intestinal tract from above downwards, almost necessarily leads us to adopt the view that the greater part of the bile is again resorbed as it passes through the intestine, and is returned to the general mass of the fluids. If a circuit of the bile from the liver through the intestine, and from thence back into the liver, appear at first sight objectless or superfluous, teleological grounds should not restrain us from the recognition of positive facts, especially when we are still very far from being able to master the aims of nature or her method of arrangement. The chief biliary constituents which are resorbed, are the soluble salts and the cholic acid liberated from its adjunct. If, as we have previously endeavoured to show, this acid is produced from fat and sugar, or solely from fat, it would be teleologically just as difficult to understand why this important element of nutrition or supporter of respiration, almost immediately after being taken, should again be given off to the external world. Whether the cholic acid be formed from fat or not, it does not at all possess the chemical constitution which true excrementitious substances usually present. In our general consideration of the animal substrata (see vol. i., p. 28), we have already mentioned that there must always be a correspondence between the chemical and the physiological qualities of a body. Now, in its chemical qualities, and especially in the numerical relations of its atomic composition, cholic acid closely resembles, and indeed is perfectly identical with the true nutritious matters and respiratory elements; for sugar, dextrin, and lactic acid are far less complex substances, far more oxidised, and far poorer in carbon, than cholic acid, and yet no one entertains a doubt regarding their physiological value in reference to nutrition and the metamorphosis of matter. We cannot perceive why cholic acid should form so striking an exception to this rule. But if we have regard to the teleological objection, according to which it seems incongruous that this substance should first be removed from the blood in order again to be taken up into that fluid, we may reply to this that many useful and likewise useless substances are repeatedly separated from the blood by the salivary and gastric glands (as we see in the case of sugar, iodide of potassium, and the salts of ammonia), and are again taken up by it. In the repeated passage of iodide of potassium through the salivary glands, no one can doubt that the relations of transudation peculiar to those organs are responsible for this phenomena. We cannot, however, ascertain what mechanical or chemical conditions in the liver, besides the formation of blood-cells, are necessary for the secretion of cholic acid in the minute biliary canals. The resorption of the cholic acid in the intestine should therefore not be deemed more unnatural or irrational than the resorption of the chloride of sodium which is separated with the bile. We are as unable to understand the special object which nature has in view in the resorption of the cholic acid, as we are to comprehend the metamorphoses which the resorbed bile appears very rapidly to undergo in the lymphatic vessels or in the blood. If it, therefore, only remains for us to assume that the resorbed cholic acid (as a respiratory element already partially consumed in the organism) contributes its part to the warming of the animal body, we have a further explanation why the perfect exclusion of bile from the intestine (in Schwann's experiments) may prove prejudicial, although very gradually, to the general health of an animal.

The Pancreatic Juice.

Notwithstanding the careful analyses of Tiedemann and Gmelin,* as well as those of Leuret and Lassaigne,† the pancreatic juice, until the last few years, has been one of the most imperfectly understood of all the fluids of the animal body; very recently, however, several excellent works have appeared on the chemical nature and the physiological function of this fluid. Bernard,‡ Frerichs,§ and lastly Bidder and Schmidt,‖ have obtained from their investigations results which, although not entirely coincident, are so decisive and certain that the function of the pancreas is now more clearly understood than even that of the liver.

The pancreatic juice is a colourless, clear, very slightly tenacious fluid, devoid of taste and smell, having an alkaline reaction, and a specific gravity ranging from 1·008 to 1·009; on heating it, there is only an inconsiderable coagulum formed, and on the addition of acids and alcohol, it only becomes slightly turbid. This secretion is so prone to decomposition, that after exposure to the air for a few hours, it developes a distinct odour of putrefaction. Frerichs found 1·36% of solid constituents in the pancreatic juice of an ass, and 1·62% in that of a dog.

We have here quoted the properties of this fluid as they have been described by Frerichs, because we have ourselves obtained similar results in an experiment made on a large mastiff; moreover, the description given by Leuret and Lassaigne agrees pretty closely with the above. On the other hand, Bernard found this fluid very viscid and tenacious, and so rich in a coagulable substance that, on the application of heat, there was entire solidification—much the same as Tiedemann and Gmelin had formerly noticed; and, in correspondence with the above reaction, there were very considerable precipitates thrown down by alcohol, acids, and metallic salts. According to Bernard, the above described very thin pancreatic fluid is only

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* Verdauung nach Versuchen. Bd. 1, S. 28.

† Recherches phys. et chim. pour servir à l'histoire de la digestion. Paris, 1825, p. 104-108.

‡ Arch. gén. de Méd. 4 Ser. T. 19, p. 68-87.

§ Op. cit. pp. 842-849.

‖ In a Private Communication.

secreted when the gland has become inflamed in consequence of the injury attendant on the operation; but since, immediately after the operation, a very thin secretion is poured forth, poor in coagulable matter, Bernard's explanation cannot hold good, and the extreme fluidity of the juice can scarcely be referred to a diseased condition of the gland in question.

In order to obtain the pancreatic fluid, we must previously give a meal to the animal to be employed, and then make an incision two or three inches in length into the linea alba, for the purpose of seeking the duodenum after the abdominal cavity has been opened; the descending portion must then (according to Frerichs) be laid open, and the mouth of Wirsung's duct sought. If, as in the human subject, the bile-duct opens at the same spot as the pancreatic duct, the former, as a matter of precaution, should be tied, while a small silver canula should be introduced from the intestine into the latter, in order to obtain this fluid in a state of purity.

Bernard attempted to obtain the pancreatic juice by establishing a fistulous opening from Wirsung's duct; with this view, he cut through the duct near the point where it enters into the duodenum, and drew the cut end towards the abdominal walls, to which he attached it by sutures.

The principal constituent of the pancreatic juice is a *substance resembling albumen or casein,* but which is not perfectly identical with albuminate of soda, with casein, or with ptyalin. It coagulates only imperfectly when heated (probably from its containing an alkali), is precipitated by acetic acid, but redissolves slowly in an excess of the acid, and especially if heat be applied; it is precipitated from its acetic-acid solution by ferrocyanide of potassium; it is precipitated by nitric acid, and if it be then boiled, especially if ammonia has been added, it assumes a deep yellow colour; on the addition of chlorine-water it separates in greyish flakes; it is thrown down by alcohol, but, according to Bernard, redissolves readily in water. Frerichs found 0·309% of this substance in the pancreatic juice of an ass. It is to this substance that the pancreatic fluid especially owes its principal chemical and physiological properties.

Bernard found a considerable quantity, and Frerichs a smaller amount (0·026%), of a *butter-like fat.*

The *organic matters soluble in alcohol* only amounted to 0·015% in the pancreatic juice of the ass.

Neither Frerichs nor Bernard could detect the presence of *sulphocyanides.*

In reference to the *mineral ingredients* (as determined by incineration), Frerichs found 1·01% in the secretion from the ass; of this amount, 0·12% was insoluble, and consisted of carbonate and phosphate of lime and magnesia, and 0·89% was soluble, consisting of chloride of sodium and alkaline phosphates and sulphates.

Nothing can be stated with any accuracy regarding the *quantitative relations of the secretion*, since the injury caused by the operation which is necessary for the purpose of observing the secretion must very much derange the physiological relations. The experiments of Frerichs merely show that it is only during digestion that the pancreatic juice is secreted. In a state of abstinence, Frerichs found the gland pale and anæmic, and the duct of Wirsung empty.

Frerichs collected 25 grammes from an ass in three-quarters of an hour, but only 3 grammes from a hound in twenty-five minutes, during the process of digestion; Bernard obtained 8 grammes from a large dog in one hour, and 16 grammes hourly after inflammation had been set up. Bernard found, as a general result, that in the latter case there was always an increased flow of the pancreatic juice, but that it ceased to be coagulable and viscid.

Diseases of the pancreas are, as is well known, extremely rare; I once found, in the duct of Wirsung, a concretion which exhibited all the characters of a protein-body, but differed from the better known salivary concretions in yielding very little carbonate and phosphate of lime, and indeed very little ash at all.

The *importance* of the pancreatic juice *in relation to digestion* was first recognized by Valentin; it converts into sugar the amylaceous matters which have not been metamorphosed by the saliva, and have passed unchanged into the duodenum. Valentin supported his opinion by the fact that the pancreas is much more developed in herbivorous than in carnivorous animals, and convinced himself that the expressed juice, or an infusion of the sliced gland, possesses in a high degree the power of converting starch into sugar. Bouchardat and Sandras* found that the juice discharged from Wirsung's duct by fowls or geese possessed this property, but lost it after being heated to 100°. They further ascertained that this property is peculiar to the nitrogenous or albuminous substance which is precipitable by alcohol, and afterwards soluble in water. More recently, this subject has been investigated with the greatest scientific accuracy by Bernard and Frerichs, to whose labours we have so often referred, as well as

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* Compt. rend. T. 20, p. 1085.

by Bidder and Schmidt; and it is now indubitably established that the pancreatic juice possesses this sugar-forming power in a far higher degree than the saliva.

Bernard claims for the pancreatic juice another and apparently a more important function; he believes that he has found that it is solely by the action of the pancreatic juice that the fat is reduced to a condition in which it can be resorbed and digested; that is to say, that it is decomposed into glycerine and a fatty acid. This view, although it appears to be supported by convincing proofs, is, however, directly opposed by the numerous and ingeniously devised independent experiments of Frerichs and of Bidder and Schmidt.

Bernard's experiments, which, strangely enough, were confirmed by the French Academy,* have reference to the following points. Both the excretory ducts of the pancreas were tied in dogs, and the animals were afterwards fed upon food abounding in fat; no milky chyle was found in the lacteals; the fat remained unchanged, and was found unaltered even in the large intestine. The following experiment appears even more decisive in favour of Bernard's opinion. If oil be injected into the stomach of a rabbit, which is afterwards allowed to partake of its ordinary food; and if it be killed three or four hours after the injection of the oil, Bernard maintains that none of the lacteals will be filled with milky chyle, except those which originate from the intestine below the opening of Wirsung's duct. This experiment would seem at the same time to show that the bile exerts no influence on the digestion of the fat, since in rabbits Wirsung's duct opens somewhat lower in the duodenum than the bile-duct. Finally, the pancreatic fluid, when shaken with fat, was said readily to form an emulsion in consequence of its viscidity, and to retain the fat in this finely comminuted state far longer than any other animal fluid; the neutral fats, however, in a short time, being decomposed into glycerine and the corresponding fatty acids.

It is singular that neither Frerichs nor Schmidt and Bidder, although their observations were made with the greatest care, have been able to confirm any one of these experiments, which Bernard maintains that he has often repeated. These experimenters have followed all Bernard's directions; after tying the pancreatic duct in cats, they have kept the animals without food for from twelve to twenty-four hours (so that it might be fairly presumed that there was no longer any pancreatic juice in the intestine), and

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* Compt. rend. T. 28, p. 960.

then fed them only with milk, fatty food, or butter, killing them in from four to eight hours after the meal. These experiments were often repeated, and the lacteals were always most beautifully injected, and the receptaculum chyli distended with milky chyle.

Frerichs performed the following experiment on puppies and cats which had fasted for a long time: he tied the small intestine far below the opening of the biliary and pancreatic ducts, and below the ligature he injected milk with olive oil, or an emulsion of oil and albumen, or pure olive oil, and he found, after two or three hours, that the lacteals were filled with white chyle. Frerichs, however, believes that he has found that the extreme comminution of the fat, and hence in some measure its resorption, are promoted by the bile and pancreatic juice; and he draws this conclusion from the following experiment:—in cats which had long fasted, he cut through the small intestine near the middle, injected olive-oil into both halves, and tied the two cut extremities; in this case, he found the lacteals springing from the upper part of the intestine always far more injected than those proceeding from the lower portion, and he referred this to the circumstance that the bile and the pancreatic juice had access to the oil in the upper part of the intestine; for although pure pancreatic juice, when shaken with oil out of the body, reduces the particles of oil to a state of extreme minuteness, the latter soon separate again on the surface.

We have already remarked in vol. 1, p. 250, that Bernard's experiment is by no means convincing on the one hand, because the chyle contains far less fatty acids than the ordinary neutral fats, and on the other hand because other animal fluids, as soon as they begin to putrefy, cause a similar decomposition of the neutral fats. Schmidt and Bidder* have, however, taken the trouble to prove in a direct manner the fallacy of Bernard's view by numerous experiments. After having fed cats with butter, they could find no trace of butyric acid in the contents of the intestine, in the chyle, in the blood, or in the bile. Hence, although decomposing pancreatic juice when in contact with butter, at a temperature of 37°, in the course of a few hours gives rise to the formation of butyric acid, no such formation of this acid occurs in the animal body. Schmidt and Bidder now tied the duodenum at its upper part, between the pylorus and the mouths of the pancreatic and biliary ducts, and by means of a pipette injected melted butter

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* Quoted by Lenz (who co-operated with Schmidt and Bidder) in his Inaugural Thesis, De adipis concoctione et absorptione. Dorp. Liv. 1850.

immediately below the ligature, but above the mouths of the ducts; in the course of six or eight hours the contents of the intestinal canal certainly contained some butyric acid; the same occurred when the ductus choledochus was at the same time tied. Hence the power which the pancreatic juice possesses in the formation of butyric acid, is impeded by the gastric juice. The converse experiment in the laboratory, with a specimen of pancreatic juice (from a large dog) at a temperature of 37°, shows that the gastric juice here acts only as a dilute acid, and may be replaced with a precisely similar result by equally diluted lactic, tartaric, or acetic acid.

Moreover, I have not found any confirmation of Bernard's experiment on rabbits (although it is one that may be easily repeated), in which he observed that after feeding them with fat, the milky injection of the lacteals could only be perceived beneath the opening of Wirsung's duct. Bidder and Schmidt have, however, discovered how Bernard was led into this error, for on injecting butter into the gullet of rabbits, they found that after two hours, the lacteals given off between the pylorus and the mouth of the pancreatic duct, were fully distended with milky chyle *very rich in fat;* if the animals were killed four hours after the injection of the fat, the lacteals situated eight or ten centimetres [about three or four inches] above the mouth of the duct were still filled; if they were killed six hours afterwards, only those below the mouth of the pancreatic duct were thus injected; and finally, if they were not killed for eight or ten hours, the first lacteals well injected with milky chyle were found to be situated from 20 to 30 centimetres [from eight to twelve inches] below the opening of the duct. Hence it must have been by always killing the animals six or eight hours after feeding them with fat, that Bernard was able apparently to maintain his view. The facts of the case were simply these. The chyle had already passed onwards from the lymphatics proceeding from the first portion of the duodenum, and there was no more fat to be absorbed in that portion of the intestine, when Bernard began the investigation.

Frerichs has also overthrown another and an earlier view of Bernard's, namely, that the pancreatic juice acidified with hydrochloric acid might take the place of the gastric juice in relation to the coagulated protein-bodies.

Lastly, Frerichs is of opinion that as the decomposition of the bile is very much hastened by the pancreatic juice, this property is of some importance in effecting the rapid conversion of the bile into insoluble products incapable of resorption.

The Intestinal Juice.

Our knowledge is very slight regarding the fluids secreted by the glandular organs of the intestinal mucous membrane. This depends in a great measure on the difficulty of obtaining these secretions isolated from the remains of food, from the secretions of the liver and the pancreas, and from the products of digestion. On this point, also, Frerichs* has thrown some light; previously to his researches, our theories on this subject were based rather on subjective views than on objective facts.

Frerichs has shown that it is in the highest degree probable that the lenticular capsules which occur in the small intestine, partly as solitary glands and partly in heaps as Peyer's glands, only contribute slightly to the formation of the intestinal juice; these lenticular glandules are, as is well known, shut sacs, which only rarely, and for the most part when in a morbid condition, burst, and thus discharge their contents on the mucous membrane of the intestine. By exposing these minute sacs to the action of the compressorium, Frerichs ascertained that they contained an alkaline fluid, which was coagulated by acetic acid, the turbidity being dependent on the presence of molecular granules and morphological elements resembling cell-nuclei. In typhus and other conditions which are associated with intumescence of Peyer's patches, and with prominence of the individual spherical capsules, the correctness of these views may be very readily confirmed. Hence Frerichs is fully justified in regarding the pouch-like glands which in the small intestine are known as the glands of Lieberkühn, and in the colon, as the follicles of the large intestine, and which occur in great numbers and are of very considerable size, as the true secreting organs of the intestinal juice. The chemical examination of the intestinal juice also shows that the fluids secreted in the small and in the large intestine are perfectly identical. Frerichs obtained this secretion for examination by applying ligatures to pieces of intestine from four to eight inches in length in cats and dogs, after having, as completely as possible, removed the contents of the gut by pressure; he then returned the intestine into the abdominal cavity, and killed the animal in four or six hours. In the piece of

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* Op. cit.

gut inclosed between the ligatures, there was then found a glassy, transparent, colourless, and tenacious mass with a strong alkaline reaction. In precisely the same manner I obtained the intestinal juice from the ileum of a man who, in consequence of a badly performed operation for hernia, had several intestinal fistulæ, with perfect inversion of a loop of gut; at one of these fistulous openings, fæcal matter appeared; at the other, pure intestinal juice might be collected. The morphological elements found in the intestinal juice are granular cells in greater or less abundance, cell-nuclei, here and there a little fat, and not unfrequently cylindrical epithelium (in the case which I examined, the latter structure was very abundant.) Notwithstanding this perfect coincidence between my experiments and those of Frerichs, which is the more striking since they were made in different ways, some recent investigations of Bidder and Schmidt* show that this subject obviously requires further elucidation; for by following the method indicated by Frerichs, these physiologists could obtain no trace of intestinal juice, so that they were compelled to postpone its examination till they could collect it from an artificially formed intestinal fistula in a dog, in whom the pancreatic juice and the bile were carried away externally by a corresponding fistula.

The gut, both in recently fed and in fasting cats, was tied immediately below the duodenum, and exactly in accordance with the directions of Frerichs. Three or four loops, at the distance of half a foot, were isolated by ligatures, and replaced; the wound in the abdomen was then stitched up, and in the course of from three to six hours, the animal was killed by strangulation. There was "not a drop" of intestinal juice to be found. In the dog from which they obtained the intestinal juice, two fistulous openings had been established, one from the gall-bladder, and the other from the small intestine to the external abdominal walls, which were perfectly healed in the course of ten days after the operation; by the introduction of silver and caoutchouc tubes, they obtained at the upper opening pure bile, and at the lower one the glandular secretion of the small intestine, mixed perhaps with a little unresorbed saliva and gastric juice, whose quantity, however, in the fasting state, would be so extremely minute as to be unworthy of notice.

The intestinal juice does not mix readily with water; it cakes, and apparently coagulates when treated with a saline solution, as an aqueous solution of chloride of sodium or sulphate of soda; the

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* In a Private Communication.

portion soluble in water behaves in precisely the same manner as the mucous juice, which will be described in a future part of this volume. Frerichs found from 2·2 to 2·6% of solid constituents in the intestinal juice, in which the parts soluble in water amounted to 0·87%, the fat to 0·195%, and the ash to 0·84%; I found only 2·156% of solid constituents.

Frerichs has not succeeded in effecting a change in any of the ordinary elements of food by means of the intestinal juice. Protein-bodies and gelatigenous substances remained perfectly unchanged; fat became disintegrated just as in all other viscid fluids. Moreover, it exerted no special action on starch; at all events, after prolonged digestion at 37°, no more boiled starch was converted into sugar than would have been obtained by the action of animal membranes, soluble albumen, casein, &c. Hence Frerichs is compelled to deny to the intestinal juice any action as a direct digestive agent; but, on the other hand, the intestinal juice which I collected from the loop of gut of the patient in our hospital, possessed in a high degree the power of converting starch into sugar; but protein-bodies and fats, whether the juice were modified or not, were so little affected by this mucus, that I must express my doubts whether it exerts any digestive action on these substances; and the more so, since cubes of coagulated albumen and pieces of flesh, when introduced into the lowermost of the fistulous openings, were expelled from the rectum almost entirely unchanged; the fistula was, however, on the lower part of the ileum, and probably near the cæcum. Bidder and Schmidt have, on the other hand, convinced themselves, by the most striking experiments, that this *intestinal juice not only metamorphoses starch* with as great rapidity as saliva and pancreatic juice, but also that *the intestine exerts as powerful a digestive influence on flesh, albumen, and the other protein-bodies, as the stomach.*

In cats that had been kept for some time without food, the duodenum was cut below the openings of the pancreatic and biliary ducts and above a cork plug, which was inserted and strongly tied into the upper end, so that the secretions of the stomach, pancreas, and liver, were absolutely excluded; in the lower end two cylinders of flesh and albumen were sewed up in muslin bags, and pushed down as far as possible, and the wound stitched to prevent their escape; the gut was then replaced, the edges of the wound in the abdomen brought together, and in the course of five or six hours the animal was killed. The muslin bags, which were found low down in the small intestine, appeared externally to be much collapsed; and, on opening them, the pieces of flesh and albumen presented a macerated appearance, as if they had been exposed to the action of gastric juice, and were strongly alkaline; the albumen was thoroughly softened and broken down, and in the twelve experiments at present made, lost from one-eleventh to one-half of its original weight, (the experiments including both albumen which had been dried at 120°, and moist specimens,) so that in the latter case the contents of the bags appeared to have almost entirely vanished. The experiment suceeeded equally well when the gastric juice was excluded, but access of the bile and pancreatic juice was allowed. The cork plug was then, of course, introduced between the pylorus and the openings of the biliary and pancreatic ducts.

The Contents of the Intestinal Canal and the Excrements.

The chemical examination of the contents of the intestinal canal has not as yet led to any very certain results; indeed, up to the most recent time, we find that different opinions are held regarding certain points which might easily be decided. We can readily understand the reason of this, when we consider the great variety of matters which must necessarily occur in the intestinal canal. We need hardly observe, that even after tolerably simple food, imperfectly digested and indigestible substances will be simultaneously found in association with already metamorphosed and decomposed matters, and that to this already very complicated mixture there are added the constituents of the digestive fluids in every stage of metamorphosis. The difficulty of the investigation lies, however, especially in the circumstance that the digested soluble substances always occur in only extremely minute quantity in those parts of the intestinal canal where they are pretty quickly resorbed. The insoluble substances in the intestinal contents are less accessible to chemical examination, and are unquestionably of less interest in relation to the study of the process of digestion. We shall here limit ourselves to a notice of the actual experiments that have been made on this subject, since the metamorphosis of food as a special process will be subsequently considered when we treat of "Digestion."

In regard to the reaction which the intestinal contents exhibit toward vegetable colours, we may remark, that an acid reaction is always apparent in the duodenum and jejunum; in the ileum it begins to diminish, so that for a great extent before we reach the cæcum, it has often entirely disappeared. As a general rule, the contents of the large intestine are alkaline; it very often, however, happens (as has been previously mentioned) that the inner portions of the contents are still strongly acid, while the outer parts, moistened or permeated with the alkaline intestinal juice, are neutral or alkaline. This acid reaction is usually dependent on the presence of lactic acid, but occasionally on that of butyric, acetic or other acids. The sources of the *lactic acid* are, however, very various, being dependent both on the nature of the food that has been taken, and on the part of the intestine from which the mass has been obtained. In the duodenum, where, notwithstanding the access of bile and pancreatic juice, a strong acid reaction is observed, the free acid depends chiefly on the acid of the gastric juice, whatever kind of food may have been taken; after the use of flesh, sour milk, or acidified food, the acid of the food naturally takes part in the reaction of the contents. In the normal state, it cannot depend on a lactic fermentation, or on any other acid fermentation, since any such fermentation is prevented by the normal gastric juice. On the other hand, it is generally only found in the lower part of the small intestine, and in the large intestine after the use of amylaceous substances; hence, we must conclude that here the reaction is not dependent on the digestive juices, but on the metamorphosed starch. That the free acid which occurs there, is lactic acid, may be readily proved by analysis (see vol. 1, p. 95). But in the normal condition both starch and sugar are converted in the ileum and the rectum into lactic acid. Moreover, as Frerichs has shown, the lactic acid sometimes becomes transformed into butyric acid in these parts, when all other relations seem perfectly normal. Among the free acids occurring in the small intestine, but exerting less influence on the reaction of its contents, we may mention cholic, glycocholic, and choloidic acids. Frerichs has very thoroughly traced the changes which the biliary constituents undergo in the intestinal canal, and has proved that in the large intestine for the most part we find only dyslysin, but sometimes also a little cholic or choloidic acid.

As a general rule we can, by means of Pettenkofer's test, trace the presence of the resinous constituents of the bile as far as the lower extremity of the ileum. (See vol. 1, p. 125.)

Among the less soluble substances which we may extract from the contents of the intestine, we very often meet with *grape-sugar* or *glucose.* This very rarely depends upon sugar having been present in the food; for it is precisely after saccharine food has been taken, that we most rarely find this substance in the small intestine, and then only in its upper part; the sugar introduced into the stomach is unquestionably resorbed from thence, being a readily soluble substance. On the other hand, the sugar found in the small intestine, and sometimes even in the large intestine, owes its origin to the action of the pancreatic juice on starch—an action which, with the co-operation of the intestinal juice, is prolonged to almost the end of the intestinal canal.

In seven cases in which Frerichs fed animals with milk, he could only twice find sugar in the jejunum.

In the aqueous extract of the contents of the small intestine, and occasionally in that obtained from the contents of the large intestine, we find a *protein-body* coagulable by heat, and usually precipitable by acetic acid, always, however, occurring in small quantity. This minute quantity of coagulable matter might well be regarded as a product of the digestion of some protein-body that had been taken as food; for the peptones, which are so readily soluble, are for the most part resorbed from the stomach itself; the digestion of the protein-bodies which pass undissolved from the stomach into the small intestine, cannot be very considerable in the small intestine after the access of the bile. Moreover, the pancreatic juice, to judge by the amount of its secretion, cannot yield any great contribution to the coagulable matter of the aqueous extract of the intestinal contents. But we also invariably find some coagulable albuminous matter after the use of vegetable food poor in protein-bodies, or even of non-nitrogenous food. Hence its sources can only be sought in the exudation of a larger or smaller quantity of albumen from the blood-vessels, in consequence of endosmotic relations.

In four cases in which fasting horses or dogs were fed for two days on balls of starch, and were then killed, I found by no means a very small quantity of coagulable matter in the aqueous extracts of the contents of the jejunum and ileum. In the discharges from the ileum in the above mentioned case of intestinal fistula, coagulable matter was always found after the use of water-gruel and other slightly nitrogenous food, and in such quantity that it could not possibly be referred to the protein contained in the bread, groats, &c. We need hardly mention that the precipitate formed on boiling must always be treated with acids and other reagents; for in the watery extract of the intestinal contents, especially in that obtained from the colon, we not unfrequently observe, on heating, a separation which does not depend on albumen, but in part on the relations of weak acid solutions of earthy salts, described in vol. 1, p. 338, and in part on the coagulation of mucus, which, if a large quantity of dissolved alkaline salts be present, is very similar to that of albumen. Frerichs has also often found albumen in the colon, and even in the rectum of young dogs and cats after the free use of an animal diet; hence, he inclines to the view, that notwithstanding the impediment which the bile may oppose to the further digestion of the coagulated protein-bodies in the intestinal canal, still, at all events, small quantities of protein-bodies are digested, or at least the modified albumen (peptone) is converted by the bile and pancreatic juice into ordinary albumen. I can by no means assert that this view is erroneous, since it is only by accurate quantitative determinations, which in this case are accompanied with much difficulty, that the point could be decided; but the facts which have been already mentioned, indicate that the coagulable matter which we so frequently meet with in the contents of the intestine, may have its origin in other sources than in the direct conversion of the ingested protein-bodies into soluble and coagulable albumen. I am able in all respects to confirm the results of the experiments of Frerichs, in which he found that soluble albumen was present even in the large intestines of young carnivorous animals, but I attribute it to the presence of undigested flesh; for the contents consisted of lumps of flesh (even when the food had been tolerably finely chopped), and the inner portions of these lumps reddened litmus, a reaction which might be fairly presumed to depend on the lactic acid originally contained in the flesh. If the alkaline intestinal juices had not neutralized the free acid, the soluble albumen in the flesh would have remained unchanged. It is in the upper part of the small intestine that we find most albumen, because it is there that the contents occur in the most diluted state, and offer the greatest facility for the absorption of albumen from the capillaries.

In the filtrate of the contents of the small intestines, we only rarely find *dextrin*, and never more than small quantities of *peptones*. (Frerichs.)

I have never been certain that I have detected dextrin; but there are always to be found small quantities of the substance formerly termed ptyalin, soluble in water, but insoluble in alcohol.

If we compare the alcoholic extracts of the different portions of the small and large intestine, we find that *biliary constituents* especially occur in them, in addition to the sugar which has been already mentioned, to the free acids, and to their alkaline salts; and if we treat these alcoholic extracts with ether, we find that this menstruum not only takes up fat, but more or less of certain substances which give the well-known biliary reaction with sugar and sulphuric acid.

That comparatively unchanged bile should be found in the contents of the duodenum is natural enough, but I have always been struck with the circumstance that biliary substances, and especially the resinous constituents, should be found in the gastric contents of slaughtered animals, and of men that have been suddenly killed. I observed this in a singularly distinct manner in the gastric contents of two horses that had for three days been fed upon starch-balls; the alcoholic extract of the gastric contents was rendered almost as strongly turbid by acetic or hydrochloric acid as that of the duodenal contents; the precipitate, when examined under the microscope, appeared in the form of small vesicular globules grouped together like grapes, which dissolved in boiling water, but resumed their original form as the solution cooled; they readily dissolved in the fixed alkalies and ammonia, as well as in alcohol, but not in ether: the ammoniacal solution, on evaporation, exhibited under the microscope dendritic groupings similar to, but somewhat thicker than those of efflorescent hydrochlorate of ammonia; the potash-solution, on the other hand, yielded crystalline forms resembling the plantain leaf. The solutions of this substance were precipitated by the basic acetate of lead, but not by the neutral acetate or by tannic acid: as it presented the biliary reaction with sugar and sulphuric acid very rapidly and beautifully, it cannot be doubted that unchanged biliary acids—at all events, glycocholic acid—were here present in the stomach as well as in the duodenum.

The further we descend in the intestinal canal, the less of these resinous acids of the bile do we find in the alcoholic extract; but a comparatively larger amount passes into the ethereal extract. Frerichs has also most carefully examined the changes which the bile undergoes in the course of the intestinal canal. We have already remarked in the first volume, that it is chiefly in the small intestine that the presence of the resinous acids of the bile can be easily detected; indeed, near the duodenum we often find bile still undecomposed, which can be recognized in the aqueous extract; the fresh bile discharged into the intestine is very rapidly decomposed by the simultaneous action of the free acid, of the easily metamorphosed protein-bodies, and of the temperature of the animal body; hence we here find only those modifications of the non-nitrogenous choloidic acid which are soluble in alcohol; while further on in the intestinal canal, the greater part of this acid, which is only soluble in alcohol, disappears, and in place of it we find an also gradually diminishing portion of biliary matter soluble in ether, namely, the cholinic and fellic acids of Berzelius, or one of the modifications of Mulder's dyslysin. In the large intestine, and in the solid excrement, I have invariably found a substance soluble only in ether, and in such small quantity that after as correct an estimate as it was possible to institute, it could not be assumed that this was all the bile which had been effused from the liver into the duodenum; but we are rather led to Liebig's view, according to which a large part of the bile is again absorbed in the course of the intestinal canal. As it may be thought that possibly the resinous biliary acids may also be converted into dyslysin which is likewise insoluble in ether, I boiled the contents of the large intestine, and the excrements of men and dogs, after a purely animal diet, with alcohol containing potash; but in the solution which I thus obtained, it was only rarely that I could recognize biliary resin, that is to say, regenerated choloidic acid, and then only mere traces of it.

I must here again direct attention to the circumstance that in testing the ethereal extract of the intestinal contents for bile, we must go to work with extreme care, lest in employing Pettenkofer's test we confound biliary matter with olein. (See page 88.)

A little *fat* is always found along the whole course of the intestinal canal; and we need hardly observe, that its quantity increases after a fatty diet. After the use of food very rich in fat, we often find such considerable quantities of fat in the solid excrements, that we may obtain a ready confirmation of the results obtained by Boussingault,* who found in experiments made on ducks, that in definite times, only certain (not very large) quantities of fat could be resorbed from the intestinal canal. Bidder and Schmidt† have recently obtained a precisely similar result in experiments on mammalia. Moreover traces of cholesterin may always be detected in the fat.

The *bile-pigment* also gradually undergoes the same changes in the intestinal canal as are observed to occur in the putrefaction or decomposition of the bile. It is only in the alcoholic, and occasionally in the aqueous extract of the contents of the small intestine, that we can induce the well-known changes of colour by the mixture of sulphuric and nitric acids; in the large intestine, the

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* Ann. de Chim. et de Phys. 3 Sér. T. 19, pp. 117-125.

† In a Private Communication.

bile-pigments in all probability occur under the same modification, which, according to Berzelius and Scherer, is to be regarded as the final product of the metamorphosis of cholepyrrhin.

Taurin has often, although not invariably, been detected by Frerichs* in the whole course of the intestinal canal, and even in the solid excrements.

The *constituents* of the intestinal canal *insoluble* in water, alcohol, and ether, fall for the most part within the domain of microscopic inquiry. They essentially consist of undigested or indigestible fragments of food. Among the undigested substances we commonly find not only fat-globules, but starch-granules, fibres of muscle, and fibrills of cellular (areolar) tissue in the excrements after the use of the corresponding articles of food. The *starch-granules* seem to be diminished in their diameter, and this diminution is the more marked the lower they are found in the intestinal canal; they usually appear fissured and lobulated, and as if some of their coats were partly or entirely dissolved; in this case their true nature can often not be detected under the microscope, unless with the aid of a solution of iodine. *Muscular fibres* are found in every phase of change; we recognise some primitive fibres unchanged in their histological formation, and parallelopipeds of the same structure, in which the striæ may be pretty clearly made out, presenting a finely punctated appearance; the longitudinal striæ are usually the most distinct; the sarcolemma has for the most part disappeared; finally, there often remains merely a tolerably hyaline mass, which can only be recognised as the remains of muscular fibre by the parallel grouping of a few prominent points. A complete solution of muscular fibre is not effected by the gastric and other digestive juices, as has also been found by Frerichs.

Fragments of bone, after being swallowed, may be always detected in the intestine and in the excrements, although a great part of them is obviously dissolved in the *primæ viæ*.

As the *histological constituents of the vegetable tissues* have the least tendency to be decomposed by the digestive juices, they are always found comparatively little changed after the use of vegetable food; cellulose is proof against all organic solvents, and hence we meet with all varieties of vegetable cells. The chlorophylle-cells remain unchanged; the parenchyma-cells are only sometimes isolated; spiral vessels may be beautifully seen in the excrements both of the higher and the lower animals. Yeast-cells are often met with after the use of pastry.

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* Op. cit. p. 841.

In addition to the fluid and solid contents of the intestinal canal, we must also refer to the *gases* occurring there. Unfortunately, however, the very few observations which we possess regarding these elastic fluids are not altogether trustworthy, since the investigations made regarding the gas contained in the intestines in cases of disease, have usually not been instituted till twenty-four hours after death. Magendie and Chevreul* are the only experimentalists who have examined the gaseous contents of the stomach and the small and large intestines of men immediately after their execution; and even these investigations cannot be regarded as altogether conclusive, since a person's knowledge that he is going to be executed in a few hours must probably somewhat disturb his digestive functions.

In the stomach of a man, after execution, Magendie and Chevreul found a gaseous mixture, consisting of atmospheric air in which a portion of the oxygen had been replaced by carbonic acid; and, besides this, they found a little hydrogen. (According to volume, this air was composed of 14% of carbonic acid, 11% of oxygen, 71·45 % of nitrogen, and 3·55% of hydrogen.) Moreover, it can hardly be doubted that this air was for the most part conveyed into the stomach from without. We have already mentioned that, in the insalivation of the food, a very appreciable quantity of air is mixed with it, and this is probably the most common mode by which atmospheric air finds its way into the stomach, although, in certain respiratory movements some air may be driven or pressed through the œsophagus, as, for instance, in the efforts which precede vomiting, as has been shown by Budge: some persons, however, possess the power of swallowing air at will, and of exciting vomiting by swallowing large quantities.

The diminution of the oxygen, and the considerable augmentation of the carbonic acid, may be referred with more probability to the interchange of these gases with those of the blood, than to processes of fermentation; this interchange is, at all events, a physical necessity, while processes of fermentation are always indicative of something abnormal in the stomach. In the case examined by Magendie and Chevreul, there certainly seems to have been a fermentation, as evidenced by the presence of hydrogen, although in small quantity, in the air.

In the dead bodies of healthy men and animals, the quantity of air found in the stomach is always extremely small; but there are various conditions in which there is an abnormal accumulation of

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* Berzelius, Lehrb. d. Ch. Bd. 9, S. 338-340.

air in the stomach, and some have even regarded this symptom as a special disease, and have termed it *pneumatosis ventriculi.* Even in healthy persons, large quantities of gas may accumulate in the stomach after the use of such kinds of food and drink as very readily undergo fermentation, as, for instance, biscuits rich in yeast, new bread, onions, garlic, radishes, raw fruit, or imperfectly fermented wine and beer, especially when taken in very large quantities. In such cases, a great excess of carbonic acid is always found in the stomach, since all these substances undergo the vinous and acetous fermentation, which is almost always preceded by the development of carbonic acid. If, however, hydrogen gas be found to occur in this air, its presence may be easily explained, since, as we have already seen, the amylacea have a strong tendency to undergo the butyric fermentation in the stomach, and this fermentation is always accompanied, as has been shown by Pelouze, Liebig, and others, by the development of hydrogen.

Accumulations of air in the stomach are especially observed in hysterical and hypochondriacal patients, who have an unnatural tendency to gulp air, in persons in whom the food is retained for too long a period in the stomach, and finally, in cases in which the secretion of the gastric juice is altogether impeded. In hysterical and hypochondriacal patients who have swallowed air, the gases evolved by eructation are, for the most part, devoid of odour, and hence it may be presumed that this air has undergone very little change, except an augmentation of carbonic acid.

In constrictions of the pylorus, as well as in chronic catarrhs, the stomach becomes filled with air, not only after the moderate use of the above mentioned articles of diet, but also after the ingestion of other varieties of food which do not usually cause any annoyance to healthy persons, or at the most only occasion accumulations of gas in the large intestine, as, for instance, milk, peas, cabbage, eggs, meat, and other animal food. In such cases the air contains only little oxygen, much carbonic acid, probably also hydrogen and carburetted hydrogen, and invariably sulphuretted hydrogen, which may be recognised by the smell of the eructations, as well as by its reaction on paper moistened with a solution of acetate of lead.

In patients suffering from typhus fever, who for a considerable time have taken neither food nor medicine, the stomach is not unfrequently found to be distended with gas: here the meteorism only comes on slowly, and its occurrence is very much favoured by the paralytic condition of the muscular coat of the stomach.

Chevillot* found from 25·2 to 27·8% (by volume) of carbonic acid, from 8·2 to 13·0% of oxygen, and from 66·8 to 59·2% of nitrogen, with mere traces of hydrogen, in gas taken from the stomach twenty-four hours after death.

In the *small intestine* we usually find far less gas than in the large intestine: in the small intestines of three persons who had been executed, Magendie and Chevreul found no oxygen, but an extraordinary abundance of hydrogen and carbonic acid (in the first case 24·39% CO_2, 20·08% N, and 55·53% H; in the second case, 40·00% CO_2, 8·85% N, and 51·15% H; and in the third case, 25·0% CO_2, 66·6% N, and 8·4% H.); Chevillot,† on the other hand, always found 2 or 3% of oxygen in the air discharged from the small intestines of the bodies of aged persons. We can easily understand how in cases of disease, and even in healthy persons, after the use of flatulent food or drink, these accumulations of gas occur more frequently than in the stomach; for on the one hand, the flatus is not so readily discharged from hence by eructation as from the stomach, and on the other, the fermentation and decomposition of the above named substances proceed here with a rapidity proportional to the length of time they have already remained in the stomach and small intestine. Constrictions of individual portions of the small intestine, and other diseases of the intestinal tube, contribute also essentially to the augmentation of these accumulations of gas.

On comparing the composition of the air from the small intestine with that of the gas obtained from the stomach, we observe in the one case a perfectly opposite relation to that which holds good in the other; we have here to deal with mere residual traces of atmospheric air, the greater portion of the gas having its source in the decomposition of nitrogenous and non-nitrogenous substances. We must, however, always bear in mind that these gases are only separated from those of the blood by permeable moist membranes, and that, for this reason, the analysis of the air never correctly expresses the gaseous products arising from the decomposition of the food. Hence it is more than probable that the symptoms of meteorism, which in children and hysterical women occasionally supervene to a dangerous extent, are not merely dependent on the mechanical contraction of the thoracic cavity (by

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* Journ. de Chim. méd. 1 Sér. T. 5, p. 596-650, and Arch. gén. de Méd. 2 Sér. T. 5, p. 285-292.

† [On referring to the Journ. de Chim. méd., we find that oxygen was only found in the small intestines *once* in fifty-four cases; in that case the proportion was from 2 to 3%.—G. E. D.]

the upward pressure of the diaphragm), but also on the transmission of certain gases into the blood. In these cases we should not so much suspect the resorption of carbonic acid as of hydrogen and its compounds. The amylacea, in undergoing butyric fermentation, which is only impeded in the intestine by the free acid of the gastric juice, yield hydrogen, which in its nascent state unites with the sulphur of the decomposed protein-bodies, and thus produces the sulphuretted hydrogen, which exerts so injurious an effect on the blood. The presence of sulphuretted hydrogen in the gaseous contents of the small intestine may, moreover, be readily perceived from the eructations which are developed in from four to eight hours after a meal. It is further worthy of notice, that these eructations of sulphuretted hydrogen are very common after the use of ferruginous preparations; it is possible that the presence of iron facilitates the conversion of the alkaline sulphates into metallic sulphides, and occasions the formation of sulphide of iron, whose decomposition by acids gives rise to the production of sulphuretted hydrogen. The formation of sulphuretted hydrogen after the use of the preparations of sulphur, is so well known an occurrence as hardly to require notice, and demands no explanation.

Gaseous accumulations are much more frequent in the large intestine, where they are often very considerable, than in the stomach and small intestine. According to Magendie and Chevreul's investigations, the oxygen has here altogether disappeared; they found from 43·5 to 70% of carbonic acid, from 18·40 to 51·03% of nitrogen, and from 5·47 to 11·6% of carburetted hydrogen: Chevillot* found in the gas contained in the large intestines of aged persons, from 23·11 to 93·00% of carbonic acid, from 2 to 3% of oxygen, from 95·2 to 90·0% of nitrogen, and 28·0% of carburetted hydrogen. In two analyses of the flatus, Marchand found 36·5 and 44·5% of carbonic acid, 29·0 and 14·0% of nitrogen, 13·5 and 15·8% of hydrogen, 22·0 and 15·5% of carburetted hydrogen, and in the latter of the cases 1·0% of sulphuretted hydrogen. It is worthy of remark that the

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* [On referring to the Journ. de Chim. méd., we find that the largest quantity of carbonic acid discovered in the digestive canal generally was from 92 to 93%, and that the mean quantity in the large intestines was 23·11%. The quantity of oxygen is not stated: Chevillot only observes that he found it in the large intestine five times in fifty-four cases. The mean quantity of nitrogen in the large intestines of twenty-seven aged persons was 73%; the maximum is not given in the memoir. In ninety-six cases, ten only afforded carburetted hydrogen; one in the small intestine, and nine in the large intestine. The greatest quantity found was 18·8%.—G. E. D.]

sulphuretted hydrogen always occurs in the gases of the large intestine in far less quantity than we should have expected from the odour. It is hardly necessary to indicate the reasons why the development of gas is always more considerable in the large than in the small intestine; for although the decomposition of the remains of the food may have begun in the ileum, it proceeds with greater rapidity in the colon, since there the fæcal mass no longer meets with any free acid to impede its further decomposition. Should, however, the contents of the large intestine be acid, this, as we have already shown, must depend on a butyric fermentation, which indeed is accompanied by a copious development of gas. We need not trouble the rational physician with a detailed notice of all those morbid conditions which lead to large accumulations of air in the cæcum and the colon; it is sufficient for us simply to mention that these accumulations of gas, which we are accustomed to term meteorism or flatulence, may either be a consequence of suppressed or perverse secretion of the intestinal juices, or of diminished contractility of the muscular coat of the intestine, of strictures and other anatomical changes of the colon, of pressure exerted by morbid tumours on the lower parts of the intestine, &c. Substances stagnating in the different parts of the colon, undergo complete putrefaction, and their products, gaseous as well as solid, are precisely the same as we observe out of the animal body. Thus, in the examination of such masses, Frerichs found substances precisely similar to those which Bopp has obtained from putrefying protein-bodies.

The early physicians believed in a secretion of gas from the walls of the intestine; to those who are at all acquainted with the law of the metamorphosis of the animal tissues and with the chemical processes of putrefaction, such an assumption is altogether unnecessary for the explanation of considerable accumulations of gas; and further, from what is known on the subject, it is very improbable that gases, such as hydrogen, carburetted hydrogen, and sulphuretted hydrogen (which latter we do not find in the blood), should pass from the general juices of the body into the intestinal canal. Magendie and Girardin* have, however, made an observation which has also been confirmed by Frerichs,† which, at all events, proves the possibility of a secretion of gas from the blood into the intestine; for if a loop of intestine in dogs, after being perfectly emptied of its contents, were tied at both ends, it

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* Recherches physiol. sur les Gaz. intestin. Paris, 1824, p. 24.

† Op. cit. p. 866.

was always found after some time to be filled with air. It is to be regretted that this air has not been analysed; it is scarcely likely that hydrogen and its gaseous compounds would be found in it.

Frerichs likewise notices an accumulation of gas, which, strictly speaking, is a sacculated emphysema in the serous coat of the gut; in the intestines of swine he has frequently observed bullæ of this sort, as large as a pea or a hazel-nut, filled with air.

Although from what has been already stated it may be readily inferred what are the substances which occur, and which must of necessity occur, in *the matters discharged by vomiting*, it yet may not be altogether superfluous to notice systematically the different characters of the *vomitus* in different conditions of disease. Unfortunately, many of the analyses which have been made are of little use: as in the diagnosis of a gastric disease, so also for a scientific investigation of vomited matter, it is especially important to know what period had elapsed since food was taken, or whether the stomach was empty. Without this knowledge no inference of any scientic value can be deduced. It is, however, much to be lamented that even at the present day pathological chemistry (as it is called) is as little based on physical diagnosis as on pathological anatomy; thus we find numerous analyses of the *vomitus* in dyspepsia,—a word unsatisfactory to every rational physician, and tending only to impede scientific inquiry. Every one must know that dyspepsia and pyrosis may accompany not only chronic gastric catarrh, but also the round (perforating) ulcer, cancer, and other primary and secondary affections of the stomach; if then no pathologico-anatomical diagnosis be made, the analysis of the matters vomited by dyspeptic patients can lead to no result; when it is impossible to make a certain diagnosis in dyspepsia or pyrosis, nothing is gained by the attempt to analyse the vomited matters. Notwithstanding the numerous, more or less accurate analyses of vomited matters, we still know very little regarding the various morphological and chemical constituents of the masses which are discharged in the various diseases of the stomach and other abdominal organs. All that is positively known may be included in a few sentences.

By far the most frequent cases are those in which the principal part of the vomited matter consists of imperfectly digested or entirely undigested food, and the chief reason of this is that the food is usually the proximate exciting cause of the antiperistaltic motion. Hence it follows that the food is more or less changed according to the time in which it has been retained in the stomach: thus in the round ulcer of the duodenum where vomiting occurs four or six hours after food has been taken, we constantly find that not only the albuminous substances, but also the amylacea, are far more changed than in perforating ulcer of the stomach; in scirrhus of the pylorus, on the other hand, they are usually less changed than in other cancerous affections of the stomach, &c. These changes which we perceive in the food must either be normal or abnormal, that is to say, in the first case we find half-digested muscular fibre, peptones, sugar, &c., changed in the manner which has been already described. These are the rarer cases, and for the most part occur when the seat of the disease which has occasioned the vomiting lies externally to the stomach, although sometimes also in cancer of the stomach. It far more frequently happens that the food, when it has remained for a prolonged period in the stomach, has undergone abnormal changes; if saccharine or amylaceous food has been taken, lactic, acetic, or butyric fermentation is induced, in which case the vomited matters have an extremely strong acid reaction and taste, and even seem to take the edge off the teeth; the nitrogenous articles of food appear, in this case, when examined under the microscope, to be but slightly changed, and at most to be only loosened in texture and rendered more transparent; matters of this nature are principally vomited in chronic gastric catarrh, but not unfrequently also in round (perforating) ulcer and in cancer of the stomach. It seems probable that in chronic catarrh of the stomach, all those kinds of fermentation may be set up in the starch, according to the nature of the secreted mucus, which we are accustomed to observe out of the animal body in the laboratory of the chemist, just as in catarrh of the urinary bladder there is sometimes a predisposition to acid and sometimes to alkaline urinary fermentation. Certain experiments made by Frerichs show that in diabetic patients there is a special tendency to the formation of sugar in the stomach. Another of his observations is even more important; he convinced himself that the colourless, viscid, ropy masses, which are sometimes ejected in abundant quantity in gastric catarrh, possess almost entirely the same properties as the gum-like substances produced by what is called mucous fermentation. It appears to depend, at all events in part, on the nature of the mucus secreted in gastric catarrh, whether the fermentation established in the amylacea be of the mucous, lactic, acetic, or butyric variety—a view which seems to correspond with our present knowledge of the exciters of these different kinds of fermentation, and with the different anatomical changes of the gastric mucous membrane and of the mucus secreted by it.

Masses in a thoroughly digested state, and at the same time in an almost putrid condition, are only vomited in cases of some anatomico-mechanical change in the intestinal canal, as strangulated hernia, volvulus, &c. Since, as we have already mentioned, yeast-fungi are sometimes found in the contents of the stomach and intestines—partly entering from without, and partly propagated within the body—it need excite no wonder that they are also found in vomited matters. The same may be said regarding the *sarcina,* whose nature and mode of occurrence, since its discovery by Goodsir,* have given rise to so many investigations and discussions. This organised being is in all probability identical with the alga, Merismopedia punctata, that had been described by Meyen,† and with the Gonium tranquillum et glaucum, referred by Ehrenberg‡ to the Bacillariæ; it forms smooth plates, consisting of a larger or smaller number of quadrupartite cells, which range from 1-300th to 1-500th of a line in diameter, are square, and resemble tied-up packets; these may be found singly in the vomited matters, but much more frequently hanging together in regular forms in fours, eights, and sixteens, so as to form larger surfaces. These algæ are not characteristic of any special disease of the stomach, either organic or functional, although they are most commonly found when the food has been retained for a considerable time in the stomach before the vomiting has occurred, as, for instance, in cancer of the stomach. Frerichs§ has frequently found the sarcina in the stomach after death, in cases in which, during life, no signs of deranged digestion had been observed; indeed, he even noticed it in a dog with a gastric fistula, and found that the digestion went on as regularly and energetically as before the appearance of these algæ. It thus appears to have no connexion with any pathological phenomena in the animal organism.

Hence the sarcina is of no diagnostic value, since neither its production nor its growth is dependent upon, or gives rise to any special morbid processes.

Frerichs has studied its development in a dog with a gastric fistula; he observed, first of all, round non-nucleated cells, generally

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* Edinburgh Med. and Surg. Journal. Vol. 57, p. 430.

† Neues System der Pflanzen. Bd. 6, S. 410.

‡ Infusorien, S. 58, Taf. 3, Fig. 3.

§ Häser's Arch. Bd. 10, S. 175-208.

isolated, but sometimes grouped two and two, and ranging from 1-400th to 1-300th of a line. The cell, which at first is transparent, gradually undergoes a superficial constriction through its centre, and this is crossed by a similar constriction at right angles; the lines deepen from the centre towards the periphery, till, finally, the cells appear to be divided into four equal parts, the separate squares ranging from 1-700th to 1-500th of a line: as each of these squares again subdivides in the same manner into four fresh squares, the original individual expands into large plates, which are intersected by rectangular lines, and are easily broken down into separate quadrupartite cells.

Hasse has also found the sarcina in evacuations from the bowels; and Heller* appears to have found it in a urinary sediment, although he does not seem certain of its identity.

Hasse and Kölliker,† Virchow,‡ and more especially Schlossberger,§ have instituted accurate chemical inquiries regarding the constitution of this body. Virchow found that the molecules of the sarcina were not changed by acetic acid, but that potash first rendered them more transparent, and subsequently caused their disintegration into amorphous granules. Hasse and Kölliker found that acids and alkalies only rendered the sarcina paler; that it dissolved when boiled in sulphuric acid; that when boiled with hydrochloric acid the larger parts separated into smaller; that in a hot solution of potash the contents partially dissolved, leaving a perfect skeleton; and finally, that the sarcina, after being treated with sulphuric acid, was only coloured yellow by iodine, but that, at a glowing heat, it was perfectly destroyed. The conclusions of Schlossberger were, that the sarcina was unaffected by water, alcohol, ether, and the fats as well as the volatile oils, and that neither organic nor dilute mineral acids apparently acted on it. When treated with iodine and sulphuric acid, in order to test for cellulose (according to Mulder's method), it exhibited no blue or greenish colour; concentrated sulphuric acid decolorised the sarcina, and rendered it very transparent; the interspaces between the greatest squares became swollen, and, on the addition of water, the larger broke into smaller parts. When the action was prolonged, it entirely dissolved; many were rendered yellow by nitric acid, only, however, when they had been previously treated with

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* Arch. f. phys. u. path. Chem. Bd. 4, S. 308, Taf. 1, fig. 5.

† Mittheil. der Zürcher naturf. Gesellsch. 1847. S. 95.

‡ Arch. f. path. Anat. Bd. 1, S. 364.

§ Arch. f. phys. Heilk. Bd. 6, S. 747-768.

a solution of potash; hence they appeared, at all events, in part to contain a protein-like constituent. But, on the other hand, Schlossberger could not obtain a blue colour with hydrochloric acid; indeed, he expresses great doubts whether there is any difference between the capsule and the contents, although Hasse and Kölliker believe that they had proved, both by hydrochloric acid and by potash, that a difference existed. Caustic potash causes the sarcina, or at all events its larger interstices, to swell. The sarcina is unaffected by alcoholic and acid fermentation.

Far more amenable to chemical investigation, and of more physiological interest, are the (generally) fluid materials which are sometimes vomited in the *fasting* state; as, for instance, in chronic catarrh of the stomach, in the round (perforating) ulcer, and in cancer of the stomach. Although the investigation of such secretions is indispensable to a right comprehension of the nature of the substances which, mixed with food, are usually vomited, we have as yet only few analyses of these gastric and intestinal secretions discharged by the mouth, and still fewer in which the diagnosis of the disease has been established. Thus, for instance, waterbrash (pyrosis) has excited the attention of physicians, and the vomited matter has been analysed, and, on one occasion, the fluid has been found alkaline, and on another strongly acid, without any regard to the pathologico-chemical process. Frerichs* has here also opened the path for further inquiry; he has ascertained that, in many forms of gastric disease, as, for instance, in the chronic gastric catarrh of drunkards, and sometimes in cancer and round (perforating) ulcer of the stomach, the salivary glands are consensually irritated, and secrete an abundance of saliva, which accumulates in the stomach, and finally induces vomiting. In such cases the vomited fluids present all the characters of saliva; they are in most cases alkaline, often however neutral, rarely acid, contained a large quantity of the sulphocyanides, and, under the requisite conditions, converted starch very rapidly into sugar.

These fluids were found by Frerichs to be slightly turbid in consequence of the presence of epithelium and fat-globules; their density varied from 1·004 to 1·007, and they contained from 0·472 to 0·688% of solid constituents; the application of heat did not much increase their turbidity; the addition of alcohol caused a separation of white flocculi, which possessed the metamorphic power on starch in a high degree; the watery solution of their

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* Op. cit.

alcoholic extracts assumed a dark blood-red tint with the per-salts of iron. Similar kinds of alkaline vomited fluids have been examined by Wright, Nasse,* and Bird.†

We very often observe a fluid, watery, vomited matter with a strong acid reaction; it occurs in the round (perforating) gastric ulcers and probably also in nervous spasm of the stomach (if such a thing actually exist). Unfortunately these fluids have been examined with so little care, that even if lactic, butyric, or acetic acid has been actually recognized in them with chemical certainty, it has not been decided whether the excess of acid is produced in the same way as in softening of the stomach in children (Elsässer) by the rapid fermentation of portions of amylaceous or sugar-forming food retained in the stomach, or whether it has accumulated in the stomach in consequence of an abnormal secretion from the gastric glands.

The fluids of this class that have been most frequently analysed are the *rice-water* matters vomited in *cholera;* both in their physical and in their chemical properties they are almost perfectly identical with the matters often vomited in uræmia; they are usually of a faint, sickly odour, and their reaction may be either acid, neutral, or alkaline; on standing, they deposit greyish white flakes, consisting of epithelial structures or intestinal mucus, while the fluid above appears clear and yellowish. With the exception of very beautiful groups of cylindrical epithelium, we find in these fluids only few organic matters; but, on the other hand, they contain a relatively large amount of inorganic salts, and especially of chloride of sodium, with a small quantity of alkaline sulphates. It entirely depends upon the stage of the disease whether the fluid is acid or alkaline; for a short time after the beginning of the disease the vomited matter is acid, and I found in it (as Hermann‡ had done) butyric and acetic acids, (and metacetonic acid was also very probably present.) When the fluid contained no remains of food, but resembled rice-water, and was acid or neutral, I constantly found *urea,* and can thus confirm the observations of Schmidt.§ If, on the other hand, the disease was further advanced, and the cerebral symptoms accompanying uræmia had set in, and if vomiting now came on, salts of ammonia, and especially the carbonate were found, and hence the fluid had an alkaline reaction. *Albumen* occurs only in very small

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* Med. Corresponzbl. rh. u. westph. Aerzte, 1844. No. 14.

† Lond. Med. Gaz. Vol. 29, p. 378, and Vol. 30, p. 931.

‡ Pogg. Ann. Bd. 22, S. 169.

§ Charakteristik der Cholera, u. s. w. S. 72.

quantities when the fluid is acid, but in larger quantities when there is an alkaline reaction.

The specific gravity of these fluids varies from 1·025 to 1·007; they contain from 0·4 to 0·6% of solid constituents, of which more than half are often inorganic. (Wittstock,[*] Mulder,[†] Andral,[‡] A. Taylor,[§] Becquerel,[||] Guterbock,[¶] Schmidt).

The albumen, regarding whose presence or absence in the cholera-dejections there has been so much discussion, can generally only be recognised by the aid of hydrochlorate of ammonia, or, if the reaction of the fluid be alkaline, by its neutralization.

Biliary matters are contained in the vomited matters under very different conditions. We most commonly find biliary matters vomited simultaneously with the remains of food; and, by a careful chemical examination, the biliary acids may be detected by Pettenkofer's test in most substances discharged by vomiting; it is also easy to understand how the contents of the small intestine, including the constituents of the bile, are ejected by antiperistaltic motion. We meet with larger quantities of bile mixed with slight remnants of food or only with gastric juice and saliva, in the matters vomited in inflammatory conditions of the abdominal organs, especially of the peritoneum, as well as in cerebral affections of an inflammatory nature; the vomited matter is then of a grass-green, or verdigris colour (*vomitus æruginosus*). The green colour of these fluids is dependent on the green modification of the bile-pigment, which is induced by the action of the free acid of the gastric juice on the brown pigment: the fluid has generally a strong acid reaction, and on the addition of sulphuric with an admixture of nitric acid, or of the latter acid alone, exhibits the most beautiful changes of colour peculiar to the bile-pigment. It usually contains no substance coagulable by heat, but saliva is present, as, at least, may be inferred from the circumstance that sulphocyanides may be detected in the alcoholic extract. As in all vomited matters, we here find pavement and cylindrical epithelium and fat-globules, in addition to saliva; the fat-globules in this case, when examined under the microscope, usually exhibit a green colour, from the presence of cholepyrrhin.

Bloody vomiting may, as is well known, be associated with very various conditions. The blood is often still fluid and of a tolerably bright colour when it is ejected very soon after its escape from

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[*] Pogg. Ann. Bd. 24, S. 525.

[†] Natuur en Scheikundig Archif. D. 1, st. 1, 1833.

[‡] Gaz. méd. 1847, p. 654.

[§] Chem. Gaz. 1849, p. 95.

[||] Arch. gén. de Méd. 4 Sér. T. 21, p. 192.

[¶] Journ. f. pr. Ch. Bd. 48, S. 780, u. 850.

the vessels; but most commonly it is of a dark brown red colour, coagulated, and mixed with fragments of food. In capillary gastric hæmorrhage, which may take its origin in various diseased conditions, as, for instance, in round (perforating) ulcer of the stomach, in gastric cancer, in hæmorrhagic erosions of the mucous membrane of the stomach, and in disturbances in the circulation in the spleen and liver, the blood is retained for a longer time in the stomach, and we then have the brown or black vomitus, having the colour of chocolate or resembling coffee-grounds, to which the earlier pathologists attached so much importance. The remains of blood-corpuscles are always to be found on examining this kind of vomitus with the microscope. Any one not trusting to his powers as a microscopist, may easily obtain a red fluid by heating the dried mass with alcohol containing sulphuric acid, in which the presence of hæmatin is indicated not merely by the general character of its solid residue, but also by the abundance of iron in the latter. Fat-globules, epithelial structures, &c., are also found in these masses.

Sugar has very often been found in vomited matters: MacGregor,* Polli,† and, more recently, Scharlau,‡ have found it in the contents of the stomachs of diabetic patients: two observations made by Frerichs,§ appear to confirm these observations; for in the matters vomited by diabetic patients after the administration of an emetic, he found a large quantity of sugar, but no dextrin. It was also worthy of remark that notwithstanding the neutralization of the acid vomited matters, no lactic fermentation could be induced.

Frerichs believes that this experiment throws some light on the pathogenesis of diabetes. Although this indication, if it turn out to be constantly exhibited, should undoubtedly not be overlooked, yet we still think that the proximate and essential cause of diabetes is hardly to be sought in the *primæ viæ;* for in the normal condition, starch is converted into sugar in the stomach, and sugar is found in the blood; moreover, sugar is formed in the liver; that is to say, it is not only found therein, as Bernard asserts, but, as I have observed, far more sugar proceeds from the liver through the hepatic veins, than is conveyed to it through the portal vein and the hepatic artery; hence, for the present, it seems more correct to assume with C. Schmidt, that in diabetes the conversion or regressive formation of the sugar is impeded. Moreover, it need not excite our wonder that a large quantity of sugar is found in the contents of the stomachs of diabetic patients, since there is

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* Lond. Med. Gaz. May, 1837.

† Omodei annali univers. 1839.

‡ Zuckerharnruhr. Berlin, 1846.

§ Op. cit. p. 804.

no improbability in the supposition that sugar is also separated by the gastric glands as well as by the salivary glands from the diabetic blood.

Nasse* has observed a remarkable case in which large quantities of *fat* were vomited. No evidence could be adduced to show that the fat had been introduced from without into the stomach.

Although the general character of the *solid excrements* in the normal state must be sufficiently obvious, from the above sketch of the changes which the individual substances undergo in the intestinal canal till they reach the rectum, we must return to the subject for the purpose of considering the pathological relations of the intestinal excretions. Important as is the investigation of this subject for physiologists, and especially for physicians, our investigations regarding it are as yet few and of doubtful accuracy. The analysis of the solid excrements is, however, attended with so many difficulties, and is so disgusting a task, that we find it exciting the complaints even of a Berzelius. Putting out of the question the repugnance which must be overcome before we can handle and apply heat to such matters, the extreme varieties which the excrements present according to the nature of the food that has been taken, and the great facility with which decomposition extends in such masses, we are hindered from making a tolerably correct analysis, by the circumstance that all solutions pass in a turbid state through the filter, and that the decomposed biliary constituents distribute themselves through all menstrua, so that we cannot readily extract a substance to which some decomposed bile-pigment or putrid biliary matter does not adhere.

An adult male, in a state of health, living on a mixed diet, usually discharges in the course of twenty-four hours from 120 to 180 grammes of semi-solid brown masses, whose unpleasant odour seems from Valentin's experiments to be far more dependent on decomposed constituents of the bile than on the remains of the food. These masses contain about 25$\frac{0}{0}$ of solid constituents, so that from 30 to 45 grammes of solid dry matter are daily carried off in the intestinal evacuations of a healthy man living on a mixed diet.

As, in our remarks on the contents of the large intestine, we have at the same time considered the constituents of the fæces, we now proceed to point out the differences which the excrements present under special physiological and pathological conditions.

It is almost unnecessary to introduce the remark that indi-

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* Med. Correspondzbl. rh. u. westph. Aerzte, 1844, Nr. 14.

gestible fragments of food, as vegetable cellular tissue, tendons, skin, &c., occur in the fæces in varying quantities according to the nature of the food, and that the amount of undecomposed bile which is found, is proportional to the rapidity with which the food passes through the intestinal canal. The examination of the properties of the meconium and of the intestinal contents of the fœtus generally, is a subject of more importance.

According to my experience, the small intestine of the *human fœtus, between the fifth and sixth month,* always contains a bright yellow mass, which is either neutral or faintly acid; its ethereal extract consists of margaric and oleic acids and saponifiable fat, and when treated with sulphuric acid and sugar, only very gradually yields a purple colour; in the alcoholic extract we may recognise taurocholate of soda, (partly by its relations towards the salts of lead, acids, and alkalies, and partly by the formation of sulphuric acid when treated with potash and nitric acid,) bile-pigment, (although not always to be detected by nitric acid,) and the chlorides of sodium and potassium. Boiling alcohol extracts from the mass, which is insoluble in the cold fluid, a substance which separates on cooling, and in its further reactions is similar to casein or albuminate of soda; the watery extract contains a substance precipitable only by tannic acid (unaffected by neutral or basic salts of lead or silver), and presents traces of alkaline sulphates. By far the greatest part of the solid materials in these cases (from 89 to 96$\frac{0}{0}$ of the dry residue) consists of insoluble matter, namely, of epithelial structures and mucus.

The contents of the *large intestine* of the fœtus in and after the seventh month, are almost perfectly similar to the *meconium* discharged after birth; they constitute dark-coloured, brownish green, almost black, tolerably compact masses devoid of odour, and without any very well-marked taste, but having a strong tendency to decomposition (as also has been observed by Höfle);* at an ordinary temperature this substance has, in the course of twenty-four hours, converted spirit of 78·8$\frac{0}{0}$ into acetic acid. As a general rule, I have found the contents of the large intestine, as well as the meconium, acid; occasionally, however, they are neutral; under the microscope the masses are found to consist essentially of epithelium and mucus-corpuscles, the epithelium presenting a beautiful green tint; ether extracts a tolerably large quantity of fat, in which, by careful evaporation, the most beautiful tablets of cholesterin may be perceived; the alcoholic extract forms a greasy

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* Chem. u. Mikrosk. 2 Aufl. S. 85.

blackish brown mass, which under the microscope exhibits no trace of crystallization; no distinct reaction either of the biliary acids (by the sulphuric acid and sugar test) or of bile-pigment (by nitric acid) could be obtained. The watery extract, even when obtained before the substance had been treated with alcohol and ether, contains no substance which is coagulable or precipitable by acetic acid; it contains, however, a nitrogenous body precipitable by tannic acid but not by metallic salts; and it yields no trace of sulphates.

The bright yellow, semi-fluid excrements of infants at the breast contain, as was shown by Simon,* a very large amount of fat, which may naturally be referred to the milk, besides much coagulated but undigested casein; the alcoholic extract, when treated with a mixture of sulphuric and nitric acid, generally gives the well-known changes of colour indicative of cholepyrrhin; and Pettenkofer's test applied to this extract usually demonstrates the presence of the biliary acids. Epithelial structures abound in these excrements.

Liebig some years ago made the remark that the solid excrements contain only a small amount of soluble salts; I found only 23·067% of soluble salts in the ash of normal human excrement; Fleitmann,† on the other hand, found 30·58% (after an abundant animal diet), and Porter‡ 31·58%; the latter chemist found that in dried normal excrements generally there are contained, on an average, 6·69% of mineral substances. The ash of human fæces contains, according to Fleitmann, 30·98%, and, according to Porter, 36·03% of phosphoric acid in combination with alkalies or earths, the acid being combined with three atoms of base; the former found only 1·13% of sulphuric acid, the latter 3·13%; it is singular that in the analyses of both these chemists, the potash preponderates in an extraordinary degree over the soda; if we deduct the chloride of sodium from the soluble constituents of the ash, the ratio of the soda to the potash in the ash is 1 : 40, according to Fleitmann, while it is only 1 : 12 according to Porter:—a difference which depends upon the nature of the food. Berzelius first directed attention to the fact that more lime than magnesia must be absorbed in the intestine, since we find in the solid excrements less lime and relatively more magnesia than in the food that has been taken; while the ratio of the lime to the magnesia in the

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* Med. Chem. Bd. 2, S. 488 [or Vol. 2, p. 369, of the English translation].

† Pogg. Ann. Bd. 76, S. 356.

‡ Ann. d. Ch. u. Pharm. Bd. 71, S. 109-115.

fæces varies according to the nature of the food, there is always a relative excess of magnesia. In 100 parts of ash Fleitmann found 21·36 of lime with 10·67 of magnesia, and Porter 26·46 of lime with 10·54 of magnesia. Hence the ratio of the magnesia to the lime in the excrements is as 1 : 2 or 2½. Alkaline chlorides occur in the excrements in very small quantity (from 1·5 to 4·4%), but carbonates are always present in the ash. Berzelius observed that sand is always mixed with the excrements, and both Fleitmann and Porter have repeatedly noticed the same fact.

The ash of the *dung of herbivorous animals* (the cow, the sheep, and the horse) has been analysed by Rogers,* and, in essential points, is the same as that of human excrement. It contains more silica and sand, but that is easily accounted for. It is worthy of remark that Rogers found scarcely any traces of alkaline carbonates in these ashes.

Very soluble salts only enter into the solid excrements in large quantity, when they excite diarrhœa; Laveran and Millon† have obtained this result with sulphate of soda and acetate of potash, and I have done so with phosphate of soda.

The presence of crystals of *phosphate of ammonia and magnesia* in human fæces, was for a time regarded as a sign of a grave disease, namely typhus; pathologists are, however, now generally of opinion that such is by no means the case, and that these crystals often occur in perfectly normal evacuations, although it is only under specially favouring conditions that they are found in large quantity. It cannot, however, be denied that, in certain diseases of the intestinal canal, in which the secretions and the contents of the bowels are especially prone to decomposition, as in typhus, cholera, and certain forms of dysentery, these triple phosphates are found in an extraordinary quantity, on examining the evacuations by means of the microscope.

We have already pointed out that, in all cases in which the food passes more rapidly than usual through the intestinal canal, a larger quantity of *undecomposed bile* is always found; hence this is the case after the use of saline and acrid purgatives, and in the simplest forms of catarrhal diarrhœa, as Pettenkofer‡ himself proved. That in jaundice, dependent on occlusion of the common biliary duct, even the products of the decomposition of the bile should not occur in the stools, is a fact scarcely requiring mention.

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* Ann. d. Ch. u. Pharm. Bd. 65, S. 85-99.

† Ann. de Chim. et de Phys. T. 12, p. 135.

‡ Ann. d. Ch. u. Pharm. Bd. 53, S. 90.

The excrements in such cases are of a dirty whitish grey colour, and develop a very disgusting, putrid odour; in other respects they do not essentially differ from normal fæces.

A *green coloration of the excrements* was formerly, and for a long time, regarded as a sign of the presence of bile; latterly, however, its presence in green stools has been altogether denied. The cases are certainly only few in which the green colour of the fæces depends on the admixture of imperfectly metamorphosed bile-pigment, and are almost entirely limited to the condition of true polycholia, which rarely occurs in adults, but is ordinarily present in *icterus neonatorum*. In these cases the cholepyrrhin, in consequence of the predominance of free acid, appears to be converted in the intestine only into that modification of the pigment which we term biliverdin. On adding nitric acid to the alcoholic extract of these stools, we obtain the ordinary reaction of bile-pigment, and with concentrated sulphuric acid and sugar we obtain indications of the presence of the resinous acids, so that no doubt can remain regarding the abundant existence of almost unchanged bile in these stools.

Every one is acquainted with the appearance of the grass-green, pulpy stools, which so frequently *follow the administration of calomel*. There have been many experiments, but far more controversial discussions, in reference to this coloration. My own investigations lead to the following conclusions:—After calomel has been taken, we always find mercury in the stools, whether they be green, or black, or of their ordinary colour; this had previously been distinctly established by Hermann,* and even more strongly by Merklein.† Höfle has likewise convinced himself of the presence of mercury in the fæces in these cases. The sulphide of mercury may be separated, by rinsing, from the evacuation, when stirred in water, as Merklein was the first to observe, and its chemical nature may be then very easily recognised; the dark colour of the sulphide of mercury, when finely comminuted, may certainly, like sulphide of iron, give rise to a light green colour with animal substances, and especially with the yellow bile-pigment; indeed, powdered calomel, when triturated with yellowish brown excrements, causes them, according to Hermann, to assume a greenish colour. But, notwithstanding these facts, we should not deny the presence of almost unchanged bile in calomel stools, for we may with facility recognise

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* De rationibus dosium calomellis, &c. Diss. inaug. Hauniæ. 1839.

† Ueber die grünen Stühle nach dem Gebrauche des Calomels im typhösen Fieber. Inauguralabhandlg. München. 1842.

the presence of bile-pigment by nitric acid, and of the resinous biliary acids, by Pettenkofer's test, in the alcoholic extract when carefully prepared; and this extract may usually be obtained in considerable quantity. Every one who himself analyses such stools is, at all events, led to the subjective conviction that a part of the green and light colour may be dependent on bile-pigment. To this we must add that Buchheim* has recently convinced himself by experiments on dogs, provided with artificial fistulous openings (made according to Schmidt and Bidder's directions) between the gall-bladder and the external abdominal walls, that the administration of calomel actually causes an increased secretion of bile, as well as a more abundant secretion of mucus. If, moreover, the administration of calomel is sometimes not followed by green stools (and this is not very unfrequently the case), the evacuations either retaining their normal colour, or presenting the characteristics of special morbid processes, this must not be regarded as presenting an argument against Merklein's view; for it is obvious that, when the intestinal canal is in an abnormal state, the conditions may not always be present which are requisite for the formation of sulphide of mercury. On the other hand, this is as little in opposition to the view that the bile-pigment takes part in the coloration, since there are various conditions under which the action of calomel on the hepatic secretion may be modified and entirely checked.

The case is altogether different with the dark, often black, but frequently also green coloured stools, which occur after the prolonged use of *preparations of iron*, or *chalybeate mineral waters*, especially such as contain sulphate of soda with carbonate of protoxide of iron. Kersten† was the first to show that the green colour of these excrements was due to sulphide of iron; his only error was that he ascribed the colour to the bisulphide, being led astray by the analogy with the formation of prismatic iron pyrites, $Fe\ S_2$, (spear pyrites,) which, as is well known, is produced in stagnating waters, when organic substances undergo putrefaction in the presence of the oxides of iron and alkaline sulphates. In three cases in which I analysed the green and black excrements of persons who for a long time had taken the Marienbad waters at their source, I‡ found 3·163%, 1·039%, and 2·100% of protosulphide of iron in the dry residue of the pulpy stools.

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* In a Private Communication.

† Walther's u. Ammon's Journ. f. Chir. Th. 3, S. 180.

‡ Göschen's Jahresber. Bd. 3, S. 42.

The watery extract of these excrements contained much sulphate of protoxide of iron, which seemed to increase in proportion to the length of time during which they were digested with water and exposed to the air. The residue of these excrements, which was insoluble in water, alcohol, and ether, developed sulphuretted hydrogen when treated with hydrochloric acid, and the acid filtered fluid gave distinct indications of iron with all the ordinary reagents. I now separated the residue insoluble in water, alcohol, and ether, into three parts; from one I extracted the iron with hydrochloric acid, treated the solution with chlorine, and determined the peroxide of iron quantitatively by precipitating it with caustic ammonia; the second part I treated with aqua regia, and determined the iron and sulphuric acid from the solution; while I incinerated the third part with carbonate and nitrate of soda: by these means I found that the iron stood to the sulphur in about the ratio of 28 : 16, which obviously corresponds to the protosulphide.

It has been doubted whether the sulphide of iron, even in the state of finest comminution, can give rise to a green colour; but we may very easily convince ourselves on this point by adding a proto-salt of iron to albumen, dissolving the precipitate by an alkali, and passing a current of sulphuretted hydrogen through the solution, or by adding a liver of sulphur.* There is then no precipitate, but the previously colourless fluid becomes of an intense steel-green colour from the sulphide of iron which is formed.

The alcoholic extract of these excrements, which was of a very faintly yellow colour, contained neither bile-pigment nor the resinous biliary acids; but in the ethereal extract, there was, in addition to fat, a substance which yielded the most distinct reaction on the addition of sugar and sulphuric acid.

In the ethereal extract, which ranged from 6 to 16% of the dried excrements, there were contained not only margarin and olein, but also butyric acid, and probably some other acids of the same group. In the dry excrements there were contained from 22 to 24% of substances soluble in alcohol, from 14·5 to 18·7% of substances soluble only in water, and from 16·6 to 26·8% of insoluble matters (remains of food, mucus, &c.) The mineral substances in these excrements, after drying, ranged from 18·4 to 27·8%, of which from 3·04 to 4·67% was sulphate of soda.

Many vegetable substances likewise communicate a more or less *green* or *black colour to the excrements.* The stools are often

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* [This term includes all soluble metallic sulphides.—G. E. D.]

green after the medicinal use of indigo; they are often black after taking bilberries or charcoal; of a light colour after the use of rhubarb, gamboge, and saffron. They are, however, also of a bright yellow colour when the bile only flows sparingly into the intestine, as in many affections of the liver.

The presence of a large quantity of *fat* in the excrements after the use of fatty food is easily accounted for, since the experiments of Boussingault, as well as those of Bidder and Schmidt, show that only a certain quantity of fat can be resorbed in the intestinal canal: the same is observed after the use of cod-liver oil. According to Heinrich,* the amount of fat in the fæces is increased by morbid action in wasting diseases, such as pulmonary phthisis, Bright's disease, and diabetes mellitus; the augmentation of fat is, however, not of constant occurrence in any of these diseases.

It has been asserted that *sugar* has been found in the excrements in cases of diabetes mellitus; its presence, however, is not constant.

The occurrence of *blood* in the fæces is very common, although it often escapes observation. In hæmorrhoids, dysenteries, and other considerable hæmorrhages of the large intestine, the presence of the blood cannot be overlooked, and, as a general rule, no manipulation or tests are requisite for its detection. If, however, the hæmorrhage is very slight, and proceeds from the stomach or small intestine, the excrements appear variously coloured, so that no conclusion regarding the admixture of blood can be drawn from the colour and general appearance of the fæces. Every one has seen the black or chocolate-coloured tar-like stools, which were formerly regarded as peculiar to melæna, but which are observed in all cases of hæmorrhage in the upper part of the intestinal canal, in round (perforating) ulcer of the stomach or duodenum, in cancer, corrosions, &c. By a microscopic examination, fragments of blood-corpuscles may always be detected in such excrements, and hæmatin may be recognised chemically by means of alcohol containing sulphuric acid; in one instance (a case of cancer) I found a large admixture of colourless blood-corpuscles or mucus-corpuscles. In typhus, green fluid or semi-fluid excrements are not very unfrequently discharged when no calomel has been administered (and, conversely, it often happens that the use of calomel in this disease is not followed by the green stools which are characteristic of this medicine); and in this case the green coloration is dependent on an admixture of blood,

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* Häser's Arch. Bd. 6, S. 306.

the same as is sometimes observed in dysentery and in the intestinal diseases of young children. Bile-pigment and the biliary acids are only rarely to be detected in any quantity in such stools by a chemical investigation; if, however, we examine a portion under the microscope, we always find distorted blood-corpuscles, some distinctly yellow, and others very pale, together with colourless cells resembling pus-corpuscles. Hence it hardly admits of a doubt that, in such excrements, the green coloration essentially depends on the blood which is distributed through it; we find, however, in other secretions which are never accompanied by an effusion of blood, especially in cases of typhus, a green colour, as, for instance, in the pulmonary expectoration, which, even in an ordinary case of pneumonia, very often assumes a colour merging strongly on green, and in which the most beautiful blood-corpuscles may be detected by the microscope.

Albumen in a coagulable state sometimes occurs in normal fæces, as has been already mentioned. It is in dysentery that it is secreted in the largest quantity from the intestine; the dejections in this disease are often so rich in albumen, that, on the addition of nitric acid, or on boiling after neutralization with ammonia, the whole fluid solidifies. Coagulable albumen is also very often found in the pulpy or fluid evacuations which sometimes occur in Bright's disease. It is constantly present in tolerably large quantity in the fluid stools in typhus. In cholera, some coagulable albumen may always be detected in the evacuations from the bowels; but here, as in the investigation of most albuminous stools, we must neutralize the fluid with acetic acid before boiling, since it generally has an alkaline reaction in consequence of the presence of more or less carbonate of ammonia, or else effect the coagulation of the albumen by nitric acid, alcohol, &c. The quantity of albumen in the intestinal dejections in cholera, is, however, far less than in typhus.

Epithelial structures occur in the stools in all cases of diarrhœa; in typhus, cholera, and dysentery, the diarrhœa causes a rapid desquamation of the epithelium, which for the most part hangs together in masses; indeed, in cholera, we often find the entire epithelial investment of individual villi.

Mucus- or *pus-corpuscles,* are seldom entirely absent in the stools in cases of diarrhœa; they occur chiefly in simple catarrhal diarrhœa; they have sometimes been found in such quantities in the evacuations, that, from the milky appearance they communicate to the latter, the term *chylorrhœa* has been applied to this class of cases. It is in the course of chronic dysentery (lientery) that this phenomenon is most commonly observed. In typhus and in cholera we always find a great number of these cells, but they are most abundant in cases of uncomplicated dysentery.

We find a *glassy mucus* conglobated in masses of various sizes in catarrhal affections of the large intestines, both when they occur primarily, and when associated with typhus. This mucus is ejected from the follicles of the colon, and the round and pale, or elongated and granular cells and nuclei, which may be recognised in it by a microscopic examination, clearly indicate its origin.

False membranes, fibrinous exudations, and shreds of gangrenous mucous membrane, are found in the evacuations in typhus, croupous dysentery, and follicular ulceration.

The various *intestinal worms, hydatids, &c.*, which sometimes occur in the evacuations, do not fall within the scope of our department.

For the clearer comprehension of the subject, we shall give a condensed view of the physical and chemical relations of the intestinal dejections in certain diseases, namely, in typhus, dysentery, and cholera.

In *typhus*, the stools are usually fluid, of a yellowish brown colour (often resembling that of dry peas), of an abominable smell, and an alkaline reaction. On allowing one of these evacuations to stand for some time, there is formed a yellowish mucous sediment, in which we may observe flocculi of undigested food, white granules, and, if catarrh of the large intestine be simultaneously present, some clots of glassy mucus. The fluid has a yellowish or pale brown, turbid appearance, and contains more or less albumen. The white granules in the sediment, which are generally about the size of a pin's head, present, under the microscope, the appearance of little more than an amorphous mass, and are probably merely a product of the intestinal ulcers; the epithelium suspended in the fluid has for the most part a yellow tinge; crystals of phosphate of ammonia and magnesia occur in the sediment in large number, and the fluid usually contains some distorted and decolorised blood-corpuscles. By means of the microscope, we very often detect *vibriones* and fungus growths of various kinds. The green colour of the stools in typhus has been already noticed. The fluid lying above the sediment contains only a little biliary matter, but a very large amount of soluble salts, and especially of chloride of sodium, in addition to more or less albumen.

At the commencement of *dysentery*, the intestinal discharges consist chiefly of epithelium, and of a fluid poor in albumen, and mixed with a little true fæcal matter; when the process assumes a well-marked croupous character, the evacuations consist chiefly of a mixture of blood and purulent matter, in which we can detect fibrinous exudations, blood-corpuscles, cylindrical epithelium, and pus-corpuscles. When the disease runs a less severe course, clots of glassy mucus from the follicles of the colon predominate; moreover, crystals of triple phosphate may always be observed; the fluid is extremely rich in albumen, being a true exudation of the blood-plasma; biliary matters may be recognised in the alcoholic extract of its solid residue by nitric acid, as well as by Pettenkofer's test.

The stools in *Asiatic cholera* have been submitted to many analyses, which, however, have led to few results, insomuch as the simultaneous characters of the blood and of the cholera-process in general, have not been taken into consideration. The only peculiarities which we find in the stools in cholera, are the above mentioned shreds of cylindrical epithelium, an extraordinary quantity of water, a little albumen, very little biliary matter, and a relatively large amount of salts, amongst which, according to the evidence of all observers, the chloride of sodium predominates, and often to such a degree as to exceed in amount all the organic matters. The rice-water appearance of such stools simply depends on the suspended epithelium. The rose-red tint which the fluid assumes on the addition of nitric acid would be characteristic of these stools, if the same were not also often observed in typhus. These evacuations contain only from 1·2 to 2·4$\frac{0}{0}$ of solid constituents. (Becquerel,* Güterbock,† Schmidt.‡)

The intimate connection of these intestinal transudations with pathologico-chemical processes in general, finds its natural place under the head of "the Metamorphoses of the Animal Tissues," and will be noticed in the third volume.

Intestinal concretions are rare in man and in carnivorous animals, but are comparatively common in herbivorous animals, and especially in the horse. They consist chiefly of phosphate of ammonia and magnesia, with some phosphate and carbonate of lime, which have deposited themselves around a fragment of undigested vegetable or animal food. Hence their quantitative

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* Arch. gén. de Méd. 4 Sér. T. 21, p. 192.

† Journ. f. pr. Ch. Bd. 48, S. 450.

‡ Charakteristik der Cholera, u. s. w. S. 79, 81.

composition presents no peculiar interest in a physiologico-chemical point of view.

The concretions termed *bezoars*, which have recently been examined with much care by Merklein and Wöhler* and by Taylor,† are of far more importance and interest. The former analysts found that bezoars might be classified according to their chemical nature, (1) into such as consist of *phosphate of lime and phosphate of ammonia and magnesia;* (2) into such as consist of *lithofellic acid;* and (3) into those formed of *ellagic* or *bezoardic acid.* It is to the last class and its consituents that the above-named chemists have especially devoted their attention.

The *bezoars consisting of ellagic acid,* which are the true oriental bezoars, have a dark olive-green and sometimes a marbled brownish colour, an oval form, a smooth surface, a concentric laminated structure, and splinter when broken; in their interior they have a foreign nucleus; their size varies from that of a bean to that of a small hen's egg. On being heated, they carbonise without fusing, and become covered with glistening yellow crystals. Like Taylor (see vol. i. p. 118), they found the bezoardic acid to be identical with the substance known as ellagic acid, but they assigned to it a somewhat different composition from that determined by Pelouze, their formula being $HO + C_{14} H_2 O_7 + 2 Aq$, while that of the French chemist was $C_7 H_2 O_4$. This acid possesses the peculiarity that in its potash-salts it oxidises very rapidly when free access of atmospheric air is allowed, so that amongst other products of decomposition, a new acid, *glauco-melanic acid* ($= C_{12} H_2 O_6$), is produced. It is worthy of remark that the last named acid, if its potash-salt be treated with water or be decomposed by hydrochloric acid, again yields ellagic acid.

The *formation of ellagic from gallic acid* during the act of digestion in animals yielding bezoars, may be explained by our assuming that two atoms of gallic acid lose three atoms of water and assimilate an atom of oxygen, as is shown in the formula, $C_{14} H_6 O_{10} - 3 HO + O = C_{14} H_2 O_7 . HO$.

Taylor has also carefully examined the intestinal concretions known as bezoars. He divides them into (1) calculi consisting of animal hairs; (2) of vegetable hairs; (3) of ellagic acid; (4) of lithofellic acid; (5) of phosphate of ammonia and magnesia; (6) of diphosphate of magnesia; (7) of diphosphate of lime; (8) of oxalate of lime; (9) of ambergris.

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* Ann. d. Ch. u. Pharm. Bd. 55, S. 129-143.

† Phil. Mag. Vol. 28, pp. 44 and 192.

Taylor describes the concretions containing ellagic acid in much the same manner as Merklein and Wöhler. These *true oriental bezoars* are not only obtained from the intestinal canal of a wild goat inhabiting the Persian province of Chorasan, but also from Babianum cynocephalum. When freshly obtained from the animal, they have about the softness of hard-boiled eggs.

The concretions consisting of lithofellic acid, probably originate, according to Taylor, in resinous matters taken in the food. Taylor suggests that this acid should be named resinobezoardic acid.

The *excrements of birds and serpents* which, mixed with the renal secretion, are discharged from these animals through the cloaca, as well as *Guano*, the *Hyraceum* or *Dasjespis* of Hyrax capensis, and the *excrements of insects*, will be fully noticed when we treat of "the urine."

Blood.

From the earliest times the blood has been made the subject of the most various hypotheses, which, however, so far harmonized together that they agreed in ascribing to this fluid the most important share in the maintenance of animal life. Moses, in accordance with the views of the ancient Egyptians, like Empedocles, placed the seat of life in the blood. This fluid therefore has in all ages played an important part in the History of Medicine. One might therefore reasonably have expected that the enquirers of modern times would have been in possession of more than sufficient empirical supports on which to establish with some degree of completeness a knowledge of this most subtle of all animal fluids; but unfortunately the methods accessible to earlier investigators were so imperfect and their modes of enquiry so widely different from those of the present day, that even the discoveries of the last century have been of little service in enlarging our views on this subject. We need hardly allude to the obstacles opposed by a mere transcendental philosophy based upon vague notions of vitality and vital forces, by a deficient knowledge of physics and even of logic, for when we call to mind, that only three quarters of a century ago oxygen was unknown to the chemist we have at once a ready explanation of the inability which formerly existed of elucidating the great mysteries of animated nature. Even physics which had solved some of the great problems of astronomy were still incapable of interpreting the phenomena of the animal organism It is only from a comparatively recent period that we can date the first moderately accurate microscopical investigations of the blood-corpuscles, and the first attempts to investigate their origin, function and destiny, or an accurate and systematic mode of analyzing the blood, &c. In the present day the investigation of the blood has been conducted with the most earnest attention and the most zealous activity; yet, notwithstanding the devotion of so much labour, the theory of the blood is yet in the first stage of its development. But it must be remembered that the mass of correctly or incorrectly observed facts and of more or less ingenious hypotheses is abundant in proportion to the recent date of a science and to its want of fixed and reliable points of support. Such has been the fate of the theory of the blood. Its right comprehension has been rendered nearly impracticable amidst the accumulation of the innumerable enquiries which have been instituted in reference to its physical and chemical relation in physiological and pathological conditions, and amidst the multifarious and contradictory views promulgated regarding its progressive and regressive metamorphosis and the functions of its various constituents individually and collectively; so that it is now alike impossible to afford a clear and succinct exposition of the theory of the blood, and to sift facts from conclusions, or the positive from the merely hypothetical. In a chemical point of view this somewhat unpromising prospect must be referred to an imperfect knowledge of the true basis of the whole enquiry; and all who have attentively followed our observations, in the first volume, on the protein-compounds, the mineral substances of the animal body, the pigments, &c., will clearly comprehend that no thorough knowledge of the blood can ever be obtained until we shall succeed in throwing some degree of light upon these obscure departments of zoo-chemistry.

The blood, as it flows in the vessels of the higher animals, is a somewhat tenacious fluid, heavier than water, and presents various shades of red; in the arteries, however, it is constantly somewhat brighter than in the veins; it is only transparent in very thin layers. Immediately after its removal from the circulation, it becomes more tenacious and gelatinous, and finally separates into a firm, dense red mass, and a clear faintly yellow fluid.

From accurate inquiries regarding the physical properties of the blood, it has been ascertained that the *specific gravity* of normal human blood averages 1·055, its physiological limits being 1·045 and 1·075; in women it is rather less than in men, and in children than in adults; in pregnant women it is even lower than in women who are not pregnant.

Nasse,* whose labours have contributed very much to our knowledge of the blood, found that its *capacity for heat* stood in an exact ratio to its density.

The *colour* of the blood, as we usually see it, may be described as a bright cherry red; it is clearer in early youth than in the fœtal state, in infancy, or in old age; it is somewhat darker in pregnant than in non-pregnant women. The use of various kinds of food and drink, bodily exercise, and other physiological relations, to a certain degree influence the depth of the blood's colour. The action of gases and other substances on the colour of the blood will be noticed in a future page.

While still warm, the blood has a peculiar *odour*, which is generally somewhat stronger in men than in women.

The blood *coagulates*, the process commencing in from two to five minutes after its abstraction, at the surface and edges, when it gradually becomes tough and gelatinous; in the course of from seven to fourteen minutes, the jelly which is thus formed has attained such a consistence that the whole mass has assumed the form of the interior of the vessel, and has lost all its fluidity. The separated substance through which the whole blood has been converted into a jelly, now begins gradually to contract, so that a great part of the fluid inclosed by it is pressed out towards the surface; this expressed fluid we name *serum*. The contraction of the gelatinising substance continues for a period varying from twelve to forty hours, during which time a dense red clot or coagulum, the *blood-clot*, is formed; this usually assumes the form of the interior of the vessel on a reduced scale; the lower part of the clot is generally darker, and the upper of a brighter red than the original uncoagulated blood. In men the coagulation proceeds more slowly, but the coagulum is denser, than in women. Arterial blood coagulates more rapidly than venous. Atmospheric air hastens the coagulation; regarding the influence of temperature on this process, there are still different opinions. By shaking, stirring, or whipping freshly-drawn blood, the coagulating substance separates in yellowish flocculi or pellets, while the fluid remains as red as the uncoagulated blood (or perhaps a little lighter in tint) and equally untransparent.

Since the times of Malpighi and Leeuwenhoek, it has been known that the blood is not a simple solution of various substances, but an emulsive fluid in which solid particles are contained in suspen-

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* Handwörterbuch der Physiol. Bd. 1, S. 79.

sion. These solid particles consist principally of the blood-corpuscles, with which, however, other formal elements are mixed, although in far less quantity. Recent *microscopic* observations have revealed to us the following facts in relation to the blood-corpuscles.

The *blood-corpuscles* or *blood-globules* are distinguished by peculiarities of form and size in every animal genus: in man they are thick, circular, slightly biconcave discs consisting of a colourless investing membrane, and red, or, in refracted light, yellow, viscid, fluid contents. Most observers at present coincide in believing that these corpuscles have, except in rare instances, no true nucleus, a very few occasionally containing an indistinct, light granule in the concave centre. The blood-corpuscles of other mammalia likewise form round discs, except those of the Camel, the Dromedary, and the Llama, which are elliptic and biconvex. In birds the corpuscles are elongated and oval, elevated in the centre, and have a sharply defined outline; in amphibia they are oval and strongly convex.

The human blood-corpuscles average about one three-hundredth of a Paris line (=0·00333‴ or 0·00752$^{\mathrm{mm}}$) in diameter. E. H. Weber and R. Wagner have shown that in the embryo these corpuscles are generally somewhat larger than in the same animal after respiration has been established. The blood-corpuscles of the mammalia approximate tolerably closely in size to those of man; they are, however, all somewhat smaller: those of the other vertebrata, and especially of the amphibia, are, however, far larger (ranging to 0·0142‴ or $\frac{1}{72}$‴); the largest occur in the blood of Proteus auguinus.

The difference in size of the blood-corpuscles of different animals, is a point of the greatest importance in the investigation of their blood, and is the more deserving of attention, since here, as in so many other cases, chemistry entirely fails us, while the microscope and micrometry yield the most decisive results. It is at present utterly impossible to tell with certainty by chemical analysis, to what species of animal a specimen of blood that may be presented to us for examination belongs. For this object various means have been devised, to which we shall, in a future page, at all events make a passing reference; but none of them yield such decisive results in the majority of cases as the microscopico-mechanical analysis. From what has been already stated, it is obvious that by the microscope, and independently of all other aid, we can readily distinguish the blood of the different classes of vertebrata. C. Schmidt* has, however, shown that by accurate

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* Die Diagnostik verdächtiger Flecke in Criminalfallen. Mitau und Leipzig, 1848.

microscopical measurements of the corpuscles, the blood of many of the mammalia can be individually detected, and distinguished from that of man. The differences in the size of the corpuscles of different animals are so very small, that the ordinary methods of measuring these minute bodies by Weber's glass micrometer or a screw micrometer, are by no means sufficient. The blood-corpuscles being vesicles or cells with an extremely thin investing membrane, are very much influenced by endosmotic currents, and it is clear that their diameters must vary with the quantity of fluid they have imbibed or given off. When the serum loses water by evaporation, a current of fluid passes out from the corpuscles to the serum; their diameter must then diminish, just as on the addition of water we see it increase. As in the ordinary methods of measuring the blood-corpuscles, gradual evaporation cannot be prevented, and the coefficient of evaporation for each special case cannot be calculated, the idea suggested itself to Schmidt of measuring the corpuscles of *dried* blood. On drying fresh blood in extremely thin layers on a glass plate, the corpuscles lie with their flat surfaces on the glass, adhere to it, and remain extended on it after drying. Schmidt has carefully ascertained by numerous measurements that the mean diameters of the blood-corpuscles in this dried and extended membrane-like state, are unaffected or only slightly diminished, that at least from 95 to 98% of the corpuscles of the blood of the same animal species are of equal size, and finally, that the corpuscles of the blood of different species of the mammalia present constant differences of size. The following are, according to Schmidt, the diameters of the blood-corpuscles in this state, expressed in millemetres:

	Mean.	Minimum.	Maximum.
Man	0·0077	0·0074	0·0080
Dog	0·0070	0·0066	0·0074
Rabbit	0·0064	0·0060	0·0070
Rat	0·0064	0·0060	0·0068
Pig	0·0062	0·0060	0·0065
Mouse	0·0061	0·0058	0·0065
Ox	0·0058	0·0054	0·0062
Cat	0·0056	0·0053	0·0060
Horse	0·0057	0·0053	0·0060
Sheep	0·0045	0·0040	0·0048

These investigations constitute the first step to the diagnosis of the blood of different kinds of animals.

Colourless blood-corpuscles, or as they have been termed, lymph-corpuscles, are constantly present in the blood, although in far less number than the coloured corpuscles: they are more globular, although not perfectly spherical, and their diameter averages $\frac{1}{200}'''$ (which $= 0{\cdot}005'''$ or $0{\cdot}01128^{mm}$); they have a granular capsule, and either a single round, or occasionally an oval or reniform nucleus, or several small nuclei heaped on one another; in consequence of their containing a larger quantity of fat, and of their being deficient in the ferruginous hæmatin, they are specifically lighter than the red corpuscles: these cells were formerly regarded by some writers as products of coagulation, but independently of their appearance under the microscope, which shows that they unquestionably are cells, we may also readily convince ourselves that they are contained pre-formed in the living blood by a microscopical examination of the circulation in the capillaries of the frog (in the web-membrane, the mesentery, or the tongue).

It is seldom, except in whipped blood, that other formal elements, namely fat-globules and the so-called fibrinous flakes (Faserstoffschollen), are detected by the microscope.

The fluid in which the blood-corpuscles are suspended, has received the names of *Liquor sanguinis, Plasma*, and *Intercellular fluid;* in the circulating blood it contains in solution, together with other matters, the substance on which the coagulation of the blood depends.

The *Clot* consists of the coagulable matter of the blood together with the blood-corpuscles, which it encloses in the process of separation; it is moistened by a varying amount of serum.

The *specific gravity* of the serum is less variable than that of the blood itself; it averages 1·028.

The blood, consequently, is divisible mechanically into three parts: the coagulating substance, the serum, and the blood-corpuscles. Hence, nature appears to aid the efforts of the chemist, who, next to a perfect chemical separation, always desires also to accomplish a mechanical separation of the constituents of the object which he is engaged in examining; but unfortunately this very circumstance constitutes one of the principal grounds which have hitherto stood in the way of a scientifically accurate analysis of the blood. The impracticability of a perfect separation of the blood-corpuscles, which are moist cells filled with water and soluble substances, from the surrounding intercellular juice, (which we shall presently examine,) always prevents the possibility of our obtaining any certain approach to the knowledge of the processes which are at work in the blood, and which principally consist in the reciprocal action of the cells contained in it, and the plasma surrounding them. In every investigation it is necessary—and in the consideration of this most important of all the fluids, it is especially the case—that we should, before all things, make it perfectly clear from what point the inquiry should be undertaken. The physiologist is aware that in the blood, the cells and the intercellular fluid uninterruptedly act upon one another, without however the reactions being perfectly equalised; we know that the intercellular fluid acts on the cells, and that the contents of the latter react on the former; in a word, we know that the contents of the cells and the intercellular fluid are different and heterogenous; for if there were not a difference between them, no reaction would be conceivable.

Hence, like the fluid in which yeast-cells are developed, and indeed like all germ-fluids, the intercellular fluid contains the material from which the cells are formed, as well as the substances which are produced by the activity of the cells or their metamorphosis and regressive formation.

This is the point of view from which the physiologist would desire that the investigation of the blood should commence; for thus only could fruitful results be expected. The chemist, however, whether designedly or undesignedly, has failed in sufficiently separating these different objects of investigation, and for the most part has treated them simply as different constituents of one and the same fluid, whilst he has regarded the most important morphological elements,—the most essential factors in the metamorphosis of the blood—merely as simple constituents of the collective mixture, and has placed them in the same chemical category with fibrin and albumen, after separating them, like the latter, from the particles with which he presumes they are only mechanically connected and intermingled. Such a chemical mode of treating the blood must be very detrimental to physiological progress, for the chemist is hardly able to obtain in a perfectly isolated state, the substance which he regards and calculates as dried corpuscles. Hence, in order not to be led astray in our view of the composition of this animal juice by the chemical difficulties of analysing the blood and of ascertaining its constituents—points which have been already often noticed in the first volume—we shall specially consider the intercellular fluid and its constituents on the one side, and the blood-cell and its contents on the other, each independently of the other. Hence, in order to make the comparison as plain as possible, we shall give in parallel columns the quantitative relations of these two great factors in the composition of the blood.

1000 parts of Blood-corpuscles contain:		1000 parts of Liquor-sanguinis contain:	
Water	688·00	Water	902·90
Solid constituents	312·00	Solid constituents	97·10
Specific gravity....	1·0885		1·028
Hæmatin	16·75	Fibrin	4·05
Globulin and cell-membrane	282·22	Albumen	78·84
Fat	2·31	Fat	1·72
Extractive matters	2·60	Extractive matters	3·94
Mineral substances (without iron)	8.12	Mineral substances	8·55
Chlorine	1·686	Chlorine	3·644
Sulphuric acid	0·066	Sulphuric acid	0·115
Phosphoric acid	1·134	Phosphoric acid	0·191
Potassium	3·328	Potassium	0·323
Sodium	1·052	Sodium	3·341
Oxygen	0·667	Oxygen	0·403
Phosphate of lime	0·114	Phosphate of lime	0·311
Phosphate of magnesia	0·073	Phosphate of magnesia	0·222

In this representation of the quantitative relations of the constituents of the principal elements of the blood, we have preferred following the experiments and deductions laid down by Schmidt* in his admirable essay; determining from our own analyses only the mean numbers for the individual constituents, and extending our comparative tables to the fat. In describing the analysis of the blood, we shall enter fully into the methods by which those numbers, which we regard as approximative determinations, have been obtained.

From what has been already stated, it follows that in our consideration of the blood we must, in the first place, regard the morphological elements, and especially the cells, as being altogether distinct from the intercellular fluid. We shall commence, then, with the blood-corpuscles. If we would not rest satisfied with the exploded conjecture that the blood-corpuscles are living beings, whose properties are dependent on a peculiar vital force, but would attempt to form a truly logical and distinct idea of them, we must endeavour to establish an intimate relation and an organic connexion between the individual phenomena which we observe in them. In accordance with the main idea that the blood-corpuscles are vesicles filled with a dark-brownish red, tenacious fluid, their individual properties must be grouped together in the most intimate relation to one another, like the edges and angles of a

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* Characteristik der Cholera. u. s. w.

crystal to its axes. Thus the colour of the red molecules of the blood is no incidental property, but, to its most delicate modifications, it results from the idea of a vesicle which is filled with red fluid; the forms and dimensions of these vesicles are essentially changed by various endosmotic influences, and thus give rise to the various shades of colour. The form, the tendency to sink, and the specific gravity, are also properties which always have a definite relation and connexion. If, therefore, we consider the physical properties of the blood-corpuscles from this point of view, we shall attain the clearest conception of their nature, and obtain the firmest basis for the support of our views regarding the mechanical metamorphosis of matter occurring between these cells and the fluid surrounding them.

One of the properties which we observe, both in whipped—*i. e.*, defibrinated blood—and also in blood on which that operation has not been performed, is the tendency of the coloured molecules of the blood to sink, to a greater or less extent, in the intercellular fluid. The difference in this *sinking tendency* of the corpuscles is often extremely striking, both in physiological and pathological conditions; this phenomenon must consequently depend on some other properties of the blood-cells. This difference was formerly ascribed to the greater or lesser specific gravity of the blood-corpuscles. It was generally believed, in accordance with the views of Nasse, that this hypothesis was confirmed by the constantly-observed fact that the colourless blood-cells did not participate in this property with the red corpuscles, which differ so essentially from every other cell-formation in the character of their contents, which are of a tenacious fluid nature, and abound in iron. To determine the value of this hypothesis by a more accurate investigation, it would be necessary to institute more accurate and comparative measurements of the density of the blood-corpuscles and of the plasma; but, unfortunately, such determinations were not so easy of attainment to the earlier investigators as they have since become through the ingenious deductions and investigations of C. Schmidt. It was, however, obvious, without such accurate measurements, that at all events the specific gravity could not be the sole cause of this sinking tendency; for it was long known that, by the addition of certain substances to the blood, the sinking of the coloured cells was accelerated, while it would naturally be expected that the intercellular fluid would have been rendered denser by holding these substances in solution, and that the assumed differences in the densities of the cells and the surrounding fluid would have been more equalized. We should *à priori* have expected the very opposite—namely, a diminished sinking tendency.

Before, however, we proceed to notice the further causes of this phenomenon, let us more closely consider the *specific gravity* of the blood-corpuscles in its relation to that of the plasma. Since we cannot so completely isolate the blood-corpuscles from the plasma as to determine their specific gravity in a direct manner, it is only by an indirect method—that is to say, by a calculation based on other determinations—that we can ascertain their density in the condition in which they exist in fresh blood. Moreover, it will be shown by a subsequent analysis of their proximate constituents, that the blood-corpuscles of different specimens of blood must have a variable specific gravity; but it might even *à priori* be inferred that their density must vary with the varying constitution of the surrounding fluid, since a continuous diffusion-current exists between the contents of the cell and the intercellular fluid. Hence the density of the blood-corpuscles will not merely vary according to the quantity of ferruginous hæmatin which they may contain, but also according to their absorption or loss, according as they are in solutions more or less concentrated than their own contents; indeed, we shall presently see that the density of the blood-cells is far more dependent on the substances which are taken up or given off by endosmosis, than on the quantity of hæmatin they may contain; for this latter is far less variable than the quantity of water, and is also partially compensated for by an augmentation or diminution of fat in the blood-cells. The blood-corpuscles of healthy human blood have a density which, in man, varies from 1·0885 to 1·0889, and in woman, from 1·0880 to 1·0886. In diseases, the density is not confined within these limits. Thus, in cholera, Schmidt found that the specific gravity of the blood-cells was increased to 1·1025 or even to 1·1027, while in dysentery it was diminished to 1·0855, in albuminuria to 1·0845, and in dropsies to 1·0819.

We are indebted to the intelligence and indefatigable perseverance of C. Schmidt* for our knowledge of the density of the blood-corpuscles, as well as for many other discoveries in relation to the blood; when, in accordance with the method presently to be given, we have determined the weight of the moist corpuscles occurring in a specimen of blood, their density may be easily found by a simple equation, as soon as the specific gravities of the serum

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* Op. cit.

and of the defibrinated blood are known. If we assume, for instance, that a specimen of blood contains 496 p.m. of moist blood-cells, besides 4 p.m. of fibrin, that the specific gravity of the serum is 1·0280, and that of the defibrinated blood 1·0574, then we may very readily determine the density of the blood-cells by the following considerations:

	996 parts of defibrinated blood	occupy the space of	941·93 parts of water.
	500 parts of serum	„ „	486·38 „
hence	496 parts of blood-cells	„ „	455·55 parts of water

and, consequently, the density of the blood-cells in this specimen of blood must be 1·0888.

We now revert to the sinking tendency of the blood-corpuscles, and its causes. If we microscopically examine a specimen of blood in which the corpuscles sink with extreme rapidity, we find, as a general rule, that the blood-discs lie with their sides in contact with those of the adjacent discs, and thus form masses resembling rolls of money (the nummular arrangement); while in blood in which the serum and clot only separate slowly, the corpuscles for the most part appear isolated. If from this it would appear, that the nummular aggregation or cohesion of the blood-corpuscles is the proximate cause of the more rapid sinking, the more remote cause must be sought in a greater viscidity of the parts in question. Henle believed that this property was especially dependent on the tenacity of the intercellular fluid, and on the viscidity of the cells that was thus induced: in accordance with a similar view, many had previously regarded a superabundance of fibrin in the blood as the cause of the cohesion of the corpuscles; but independently of the circumstance that numerous observations (made with the view of deciding the question) prove that there is no connexion whatever between the rapidity with which the corpuscles sink and the proportion of fibrin in the blood, the perfect inertness of the fibrin in relation to this phenomenon is indicated by the fact that the corpuscles sink just as rapidly or just as slowly in defibrinated blood as in blood which contains its fibrin.

Hence the fibrin, at all events, exerts no influence on this phenomenon. There then seemed to be a tendency to ascribe the cohesion of the corpuscles to a great excess of albumen. In favour of this hypothesis the following facts were adduced, namely, that the addition of albumen or of other viscid solutions, as, for instance, of sugar and gum, hastens the sinking of the blood-corpuscles, and that horses' blood, in which the cells sink with unparalleled rapidity, contains an especially viscid and tenacious serum. Whatever probability this view might at first sight appear to possess, it will not bear a closer scrutiny: inflammatory blood, in which we most frequently observe an increased rapidity in the sinking of the red corpuscles, never contains an excess of albumen, but, on the contrary, generally contains less than normal blood; solutions of sugar and gum hasten the sinking of the corpuscles, but deprive them of their property of cohering; and lastly, the corpuscles of horses' blood sink in the serum of human or other animal blood with almost the same rapidity as in their own serum; whilst the corpuscles of other animals, when placed in the serum of horses' blood, do not by any means exhibit a great tendency to sink. Generally speaking, physical considerations do not appear to support this view. For if the viscidity of a fluid depends on the amount of attraction which its molecules exhibit towards each other, the cohesion of the particles of fluid must overcome the adhesion to the cell-walls; hence no cohesion of the blood-cells can be directly dependent on the viscidity of the fluid; but if the viscidity of the fluid consists in the fact that its molecules exhibit a greater attraction to the cell-walls than to one another, every cell must be surrounded by a sphere of fluid by which its closer contact with other cells (and consequently the aggregation of the cells generally) is prevented; moreover, we find that in emulsions the aggregation of the suspended molecules diminishes in proportion to the tenacity and viscidity of the emulsive solution. Hence Nasse was led to seek the cause of this aggregation, not in the fluid, but in the corpuscles themselves—that is to say, in a viscid property of their capsules; he referred especially to the action of carbonic acid. An abundance of carbonic acid in the blood (whether caused by an imperfect interchange of gases in the lungs, or artificially introduced into it,) is certainly usually accompanied by a rapid sinking of the blood-corpuscles. But that the membrane of the blood-corpuscle, or that its contents should actually be rendered more viscid by carbonic acid, would not be inferred from the converse experiment that oxygen and salts communicated to the blood-corpuscles a clearly defined, smooth, although often folded surface; for a solution of sugar acts on the form of the corpuscles, as far as the change can be followed by the microscope, in just the same manner as salts, and yet induces a rapid sinking of the red blood-cells. Moreover, it is hardly probable that carbonic acid should render the blood-cells viscid, and tend to make them assume the nummular arrangement, since we may very readily observe in fresh blood the commencement and gradual formation of these rolls of corpuscles under the miscroscope; in the minute drops which we use for microscopical observation any excess of carbonic acid would disappear in the process of manipulation, and in every case more oxygen would be taken up than is contained in fresh blood. Hence each of these three different modes of explaining the tendency of the blood-corpuscles to sink is opposed by definite facts which at present do not allow of any satisfactory explanation of the phenomenon. Only this much appears to be distinctly established, that, in addition to the influence exerted by the relative density of the corpuscles and the serum, their viscidity must essentially promote their aggregation. Moreover, we never observe this cohesion or peculiar aggregation of the red cells in the blood while still circulating. The tendency of the red corpuscles to sink is usually very distinctly observed in the blood of persons with inflammatory diseases, or in such blood as contains a diminution of the salts and a relative increase of the albumen. A great sinking tendency of the blood-cells is very often accompanied by a watery *liquor sanguinis*. When the blood-corpuscles are dark-coloured (and may therefore be regarded as rich in hæmatin or iron), they have a tendency to sink very rapidly, and to form nummular rolls; when they are of a pale colour (and are rich in fat), they only sink slowly. The blood-corpuscles of the horse, which sink more rapidly than those of any other animal, are comparatively poor in fat. Repeated venesections increase the tendency of the blood-cells to sink; they then become richer in hæmatin, as has been shown by C. Schmidt; they have thus become relatively heavier, and therefore sink more readily; the increase of hæmatin in the corpuscles is here certainly only relative; in consequence of the diluted plasma, an excess of globulin is abstracted from the blood-cells, which thus become comparatively richer in hæmatin, and poorer in globulin. If we consider these facts—and we shall presently notice some additional ones—we certainly feel inclined to ascribe a greater influence than we formerly did to the difference of the densities of the blood-cells and the intercellular fluid, in relation to the sinking of the corpuscles.

In special cases several conditions are often simultaneously present, which exert an accelerating or impeding influence on the sinking of the blood-corpuscles; thus, for instance, the coloured cells of the blood of the hepatic veins of the horse sink very little, while those of the blood of the portal vein (simultaneously collected from the same animal) possess a very considerable sinking tendency; this may be very readily explained by the preceding observations; the difference between the density of the cells and of the serum is far more considerable in portal blood than in that of the hepatic veins; in the former, according to my experiments, the density of the serum is to that of the cells as 1 : 1·062, and in the latter as 1 : 1·053. The serum of the blood from the hepatic veins contains (relatively to the other constituents) far less albumen than that of the portal vein; and, lastly, the corpuscles of the former blood are far poorer in hæmatin than those of the latter.

It is moreover not impossible that, at all events in certain cases, there is a converse relation of the causal action to that which we have hitherto assumed; for it is quite conceivable that the sinking of the cells is less dependent on their adhesion, than the adhesion on the gravity of the corpuscles: the viscidity of the cells can at all events not be great; for the slightest mechanical actions are sufficient to break up the nummular rolls and their branches into fragments consisting only of a few cells, which, if there were any considerable degree of viscidity, would be impossible. We may regard the following as the order in which the phenomena occur: a more or less active motion is excited in the molecules of the blood, by the difference in the gravity of the blood-cells and the intercellular fluid; and the more active the motion is, so much the more frequently will the cells be pressed together, and have the opportunity of cohering, in the same manner that a fresh precipitate, as, for instance, of chloride of silver, conglobates much more readily when the fluid and the precipitate are well stirred. If an approximation of the blood-corpuscles is rendered possible by the motion excited in the above mentioned manner, these discoid bodies can scarcely attract and adhere to each other, except by their surfaces; and that the plasma subsequently would offer less resistance to the sinking of the rolls than to that of the individual corpuscles, might be inferred from the analogous case of the chloride of silver, even if it were not obvious from physical laws. Nothing, however, but an extensive series of comparisons between the density of the blood-cells and that of the plasma, and a combination of these results with the observed sinking tendency, can enable us to come to a certain decision regarding this view: at present we must, at all events, assign to the density a considerable part of the sinking tendency of the blood-cells.

According to Nasse, the tendency of the blood-corpuscles of different animals to sink, decreases in the following order: the horse, the cat, the dog, the rabbit, the goat, the sheep, the ox, birds, the pig; so that in the horse the corpuscles sink the most rapidly, and in the pig (at all events in the winter) the most slowly.

As the density and form of the blood-cells stand in definite relations to their sinking tendency, so also is there a certain dependence between the *colour* of the blood-corpuscles and their form.

It has been already shown (in the first volume), that the colouring matter of the blood exists only in the cells, and that consequently the colour of the blood is primarily dependent on the blood-cells. In reference to the colour of the individual blood-cells, we always remark, on a careful microscopic examination, some which are paler and darker than the rest, although the number of those presenting an intermediate tint very greatly preponderates; in the blood of the portal vein, we always find some which have a speckled appearance, showing that the pigment is not distributed uniformly in them, as in all other blood-corpuscles. This difference, therefore, depends upon the absolute amount of hæmatin which they contain; but the colour of the cells must be relatively pale or intense, according as they are dilated or collapsed by the absorption or the loss of water. The gases, especially oxygen, probably exert a chemical action on the pigment, and thus influence the coloration of the corpuscles. The colour of the individual cells has, however, only a secondary influence on the coloration of the mass of the blood, but the peculiar tint of the blood is especially modified by their number as well as their form. It need scarcely be remarked, that blood which is poor in corpuscles is of a bright red colour, while blood which is rich in them must be of a darker colour; but notwithstanding this, it by no means happens (as is shown by the beautiful investigations of Popp) that blood which is poor in cells, should invariably be pale, and that blood abounding in them should be dark-coloured. Hence there must exist yet other causes which exert an essential influence on the colour of the mass of the blood—causes even more important than the colour and number of the cells. We are indebted to the genius of a Henle, for the first indication of the connexion between the colour of the mass of the blood and the form of the red corpuscles. We had been previously satisfied with the idea, that everything relating to the colour of the blood pertained to chemistry, which however could yield no information on the point. The striking changes which are induced in the colour of the blood by (chemically speaking) very indifferent substances, as, for instance, sugar and neutral alkaline salts, soon led observers to support Henle's view, and amongst them we must name one of the first of our hæmatologists, H. Nasse. If we dilute blood with water, it assumes a dark red colour; if the blood were previously dark-coloured, it becomes still darker on the addition of water; if, in these cases, we examine the blood-corpuscles under the microscope, we find them distended, and observe that they have almost lost their discoid form and become spherical; the blood collectively must therefore appear darker, since each individual corpuscle has become converted into a spherical mirror, from which the red rays are scattered and reflected. We observe the reverse on treating the blood with neutral salts, syrup, or in short, any such substances as render the intercellular fluid relatively denser: a diffusion-current is established from the cells towards the intercellular fluid, in consequence of which, the former must collapse. A microscopic examination shows us that the collapse of the corpuscles by exosmosis causes the central depression to become more considerable, and the individual cells to resemble concave mirrors. It is believed that the lighter colour of such blood must be referred to the reflection of the red rays.

Scherer,* who has very carefully studied this influence of the form of the cells on the colour of the blood, indicates also another physical cause, which exerts an influence on its coloration. The change in the form of the cells must be accompanied by a thickening or an attenuation of the investing membrane. It is obvious that when the capsule becomes thinner by the expansion of the blood-corpuscles, the pigment must shine through more in its natural, that is to say, its dark red colour, and consequently, must impart a dark coloration to the mass of the blood; and that when the corpuscles are diminished, their capsules must become thickened or thrown into folds, and must thus to a certain degree conceal the true colour of the hæmatin. In a somewhat similar manner, Mulder believes that the reason why arterial appears of a lighter red colour than venous blood, is, that the corpuscles of the former are surrounded by a dense layer of binoxide of protein, while those of the latter possess a thinner investing membrane. Hence Mulder agrees with von Baumhauer in the belief that alkalies and dilute mineral acids communicate a dark colour to the blood, since they swell up the investing membrane, which is rich in binoxide of protein, and thus render it more transparent; the

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* Zeitschr. f. rat. Med. Bd. 1, S. 288.

dark colour of the blood of the portal vein is therefore owing to the quantity of alkali contained in it.

Notwithstanding the praiseworthy investigations which have been carried on in reference to this subject, and have elicited many facts confirmatory of the above-mentioned views, the study of the changes which the colour of the blood undergoes, in consequence of alterations in the form of the cells, seems still to demand a more searching inquiry. Harless has already made a very promising beginning in reference to this subject. He has examined the influence of gases on the blood-cells, and although he merely experimented on the large, elliptical, biconvex corpuscles of the frog, he has not only confirmed several former observations, but has likewise thrown unexpected light on several points in connexion with this question. Thus for instance, we formerly ascribed to oxygen solely a chemical part in its action on the colour of the blood, although it was known that it could be removed from the blood in a mechanical way, namely, by diffusion in other gases, or by the air-pump; but Nasse, Scherer, and Harless have obtained actual proofs of the accuracy of Henle's assumption, that both oxygen and carbonic acid give rise to changes in the form of the blood-corpuscles, on which the brighter or the darker redness of the mass of the blood depends.

Although Müller did not expect that oxygen and carbonic acid would exert any visible action on the form of the blood-corpuscles, H. Nasse asserted that he had found, from often repeated experiments, that the discoid corpuscles of the mammalia become more opaque in their centre by carbonic acid, that the outer edge becomes broader, and that thus the whole vesicle swells, while after the action of oxygen the central depressions of the cells, as wells as their outlines, become more distinct; and this statement is completely borne out by the observations made by Harless on the blood-corpuscles of frogs; after the action of oxygen on frogs' blood, he found the long diameter of the corpuscles $= 0{\cdot}011'''$, the transverse diameter $= 0{\cdot}009'''$, their form strongly elliptical, their outlines dark, the cell-wall very finely granular, the nucleus of a roundish oval form but not very distinct, and the contents of a pale yellow colour; while after the application of carbonic acid, the long diameter was increased to $0{\cdot}014'''$, and the transverse diameter to $0{\cdot}097'''$, the form was almost spherical, the capsule as clear as glass, the nucleus distinct and with a sharp outline, and the contents redder than in the previous experiment.

The simultaneous action of the neutral alkaline salts, and of several other chemically indifferent bodies, on the form of the corpuscles and the colour of the blood, has certainly been already carefully examined from various points of view, but notwithstanding this, the subject still requires a systematic investigation, in order to establish definite relations between the form of the blood-cells and the colour of the blood in connexion with the amount of concentration of the solutions, the temperature, and other external conditions. For the changes which the forms of the blood-corpuscles undergo are not limited merely, according to the laws of diffusion, to a simple spherical expansion, or to a flattening and a deeper central depression, but in blood obtained during disease we very often find flatly-pressed, jagged, indented and granular, or altogether distorted yellow corpuscles, and we also observe similar modifications induced by the artificial addition of various concentrated solutions of chemically indifferent substances. At present, not even an ideal connexion has been established regarding the influence which the form of these jagged, star-shaped corpuscles or the nummular rolls exert on the colour of the blood; indeed objectively the colour co-existing with such forms has not been sufficiently observed. In reality this only is established, that all substances which dissolve or in any way destroy the investing membrane of the blood-corpuscles, or which cause it to burst, so that their contents become mixed with the intercellular fluid, communicate an intensely dark brownish red or almost black colour to the blood; while, on the other hand, all those which cause a shrivelling of the cells, or a folding or thickening of the investing membrane, give to the blood a lighter red colour, indeed during the first moments of their action almost a vermilion tint.

Henle was correct in his assertion, that in fresh blood, even when there is no disease, we observe other forms than those usually presented by the blood-corpuscles, and that in some specimens of blood the corpuscles more readily assume a jagged form than in others. This alteration of form is therefore only a consequence of influences which act on the blood submitted to examination; the predisposition to this change of form varies, however, in different blood, just as the urine in various acute diseases may be earlier or later in assuming its acid character and in depositing crystals of uric acid. All that we know regarding the manner in which the blood-corpuscles become jagged or dentated is, that chloride of sodium often induces a similar change of form in normal blood, and that a great concentration of the intercellular fluid promotes the formation of such forms; thus a drop of blood, when it has remained on the stage, and the water has in part evaporated, exhibits these jagged corpuscles; we usually observe the same appearance in the very saline sputa of catarrhal and phthisical patients, if hæmoptysis be present.

In the *portal blood* of an animal, immediately after it has been killed, we not unfrequently find (according to Schmidt) distorted and jagged bodies of this nature, but they do not occur in the blood of the hepatic veins: this difference may possibly depend on the difference in the quantity of salt contained in the serum of the two kinds of blood; for the serum of the portal blood is richer in chloride of sodium than that of other venous blood, even when the former is of comparatively low density.

With regard to the different substances which simultaneously act on the form of the cells and the colour of the blood, we shall here only briefly give the results which we have ourselves obtained, since the statements of different authors present great discrepancies in many points, as might easily be expected.

Amongst the most striking of these phenomena is the expansion of the corpuscles and the simultaneous darkening of the blood on the addition of various quantities of *water*. The swelling of the lenticular blood-corpuscles is proportional to the quantity of water which is added; they swell, however, in one diameter more than in the other; their concavity on each side disappears, and is replaced by a convexity, so that finally they become converted into spherical vesicles. These often appear to the eye smaller than the pre-existing discs, since it is little more than their transverse diameter that is enlarged, while their long diameter is diminished, if at least only small quantities of water are added. The corpuscles are then very similar to fat globules, except that they are less glistening and less distinct in outline, as if they had been faintly breathed upon. When the corpuscles have absorbed a large quantity of water, their coefficient of refraction approximates so closely to that of the intercellular fluid, that they can no longer be perceived through the microscope. By the addition of salts to this fluid the blood-corpuscles may again become apparent in their normal form; for the most part, however, they then appear distorted, jagged, or star-shaped. If the blood has been treated with a very large quantity of water, the cell-wall completely bursts, and of course no addition of salts can then restore the integrity of the corpuscles; they then form transparent, granular conglomerations, which may be rendered visible by being treated with a watery solution of iodine, as they then assume a brown colour. Blood-corpuscles which have escaped destruction may also be made again visible in watered blood, since the solution of iodine contracts the cell-wall, and gives it a yellow colour. The more we add water to whipped blood, the *darker* it becomes in reflected light, but at the same time it becomes *translucent;* while the addition of salt renders the fluid turbid and again opaque, and communicates a light red tint to it,—a fact whose physical explanation does not require notice in the present place.

The following experiments refer solely to calves' blood. The saline solutions were for the most part applied in the state of saturation at + 15°.

In relation to the action of *ether,* Nasse remarks that it renders the blood-cells smaller and paler, and he believes that a great part of the pigment is extracted by it. The mere results of my experiments on this subject are as follows:

When 100 volumes of blood were shaken with 4·8 volumes of ether, no visible darkening of the blood could be detected; the ether did not again separate from the blood; the blood-corpuscles preserved their form. After 18 hours they slightly sank, but the serum was not yellower than that of calves' blood in general; many corpuscles were then spherical, and some were distorted and had partially lost their sharpness of outline.

On shaking 100 volumes of blood with 8·1 volumes of ether, the blood became decidedly darker; the ether, however, in this case, did not again separate; most of the coloured cells disappeared, but those which could still be detected were sharply outlined, spherical, and faintly clouded on their surface; the colourless cells were very distinct.

On mixing 100 volumes of blood with from 12·4 to 24·6 volumes of ether, a dark brown red, transparent fluid was obtained; here also no ether appeared on the surface, but there was a separation of a light yellowish sediment, which, when examined under the microscope, presented the appearance of coagulated matter (shreds of the membrane forming the cell-walls); only isolated coloured corpuscles were seen, and they were pale and distended so as to resemble fat-globules; the colourless cells were as distinct as if the blood had been treated with water.

When equal volumes of blood and ether were mixed, the fluid became very dark, but highly transparent; on standing, a great part of the ether again separated from the blood; here, also, there was a deposition of yellowish flocculi; under the microscope the colourless cells appeared very distinct, but there was scarcely any trace of perfect coloured corpuscles; moreover, many large *white* globules of ether were seen in the yellow fluid; the ether collected, after 18 hours, from the watery fluid was colourless even after repeated shakings; from this I drew the conclusion that the ether had not extracted much fat containing hæmatin from the blood-cells.

Salts, such as the sulphates of soda and potash, nitrate and chlorate of potash, and similar compounds, resemble one another considerably in their action; we shall consequently limit ourselves to noticing the relations of the following, which, in this point of view, may be regarded as representatives of the neutral salts of the fixed alkalies.

On mixing 1 volume of blood with 0·8 of a volume of a solution of *nitrate of soda* (saturated at 15°), a light vermilion-coloured opaque fluid resulted, in which the blood-corpuscles were strongly contracted in their centre, and had a biscuit-like* or drum-stick-shaped form. After 24 hours (at 12°), the corpuscles had sunk to the extent of 1-22nd of the volume of the fluid; the serum did not separate very completely from the clot, and the whole of it had a somewhat reddish tint; the colour of the whole blood had again become somewhat darker, so as to resemble that of unmixed blood; the blood-corpuscles presented very great differences in size and form, and were spherical, angular, elongated, and jagged.

When 100 volumes of blood were mixed with 64·7 volumes of a solution of common *phosphate of soda*, the resulting fluid was of a light vermilion colour, and after 45 minutes the corpuscles began to sink; these were strongly contracted and biscuit-formed; after 23 hours the coloured cells had sunk to the extent of about 1-16th of the volume of the fluid; the serum was perfectly colourless, and the clot was of a bright scarlet tint; the corpuscles were still strongly contracted.

On mixing 1 volume of blood with half a volume of a solution of *protocarbonate of soda*, a very light vermilion-coloured fluid was obtained; in the course of 40 minutes the corpuscles had distinctly sunk; they were considerably contracted. After 24 hours they had sunk through 1-15th of the volume of the fluid; the colour of the blood was very dark; the serum was reddish, imperceptibly verging into the clot, and very tenacious and viscid; the blood-corpuscles were spherical, pale, and clouded.

On mixing 1 volume of blood with 0·7 of a volume of a solution

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* [*Backschüssel-biscuit* in the German.—G. E. D.]

of *bicarbonate of soda,* a very light vermilion-coloured fluid was obtained; the blood-corpuscles were very much contracted, and, after 35 minutes, began to sink. After 24 hours the colour was still of an equally light red, the blood-corpuscles had sunk to the extent of about 1-10th of the volume, and the serum was clear and colourless.

1 volume of blood mixed with 0·8 of a volume of a solution of *ferrocyanide of potassium,* presented precisely the same characters as the preceding mixture; the corpuscles began to sink after 50 minutes. After 18 hours about 1-18th of the volume of the serum was clear and colourless.

1 volume of blood, on the addition of 0·7 of a volume of a solution of *borax,* became of a very light red colour; the blood-corpuscles were contracted to almost the same extent as by the previous salts, and, after 24 hours, had sunk to the extent of about 1-15th of the volume of the fluid; the serum was clear, but reddish.

Blood treated with half its volume of a solution of *iodide of potassium* became of a light vermilion colour, and its corpuscles were much contracted and biscuit-shaped; they began to sink in the course of an hour. After 18 hours they had sunk to the extent of about 1-25th of the volume of the fluid; the serum was reddish and turbid, and very distinctly separated from the clot; the whole fluid was of rather a darker red than fresh unmixed blood; it was, moreover, gelatinous and ropy; the blood-corpuscles had lost their discoid shape, and were spherical, but were much smaller than previously, and some of them were very much distorted and jagged.

100 volumes of blood assumed a light vermilion colour on being mixed with 44 volumes of a solution of *sulphocyanide of potassium;* the blood-corpuscles were contracted, and began to sink in the course of 34 minutes. In 24 hours the fluid assumed a blackish brown colour; the corpuscles had now only sunk through 1-10th of the volume, but at the same time the serum was reddish and transparent; the clot formed a dark blackish brown, transparent, clear, perfectly liquid mass, in which no morphological element could be recognised with the microscope.

On the addition of 0·6 of a volume of a solution of *chloride of calcium* (1 part of the salt to 12 of water) to 1 volume of blood, a light red colour was produced, although not so light as with most of the alkaline salts; after an hour the blood-corpuscles began to sink and to contract. After 18 hours there was no further trace of sinking; the corpuscles were then enlarged in their long diameter, and very much diminished in thickness, so that they resembled lamellæ rather than discs; moreover, they were very much distorted, and some of them had a jagged appearance.

1 volume of blood, mixed with half a volume of a solution of *sulphate of magnesia*, became of a light vermilion colour, and remained so even after 18 hours; the fluid had then become very ropy; there was very little sinking of the corpuscles, which had assumed a biscuit-like form and had their long diameter increased; their discoid form was somewhat distorted, and they were often a little jagged at the edges.

On treating 1 volume of blood with two-thirds of a volume of a solution of *hydrochlorate of ammonia*, it first assumed a vermilion colour, but, after 24 hours, appeared far darker than blood treated with sulphate of soda, although scarcely darker than unmixed blood; after 1 hour and 5 minutes the corpuscles began to sink, but after 10 hours, there was no true separation of serum; on the surface the mixture was red, and only slightly transparent; it was, moreover, very ropy. The corpuscles were spherical, and smaller in diameter than the original discs.

1 volume of blood, when mixed with half a volume of solution of *cane-sugar* (1 part of sugar to 22 parts of water), became of a somewhat lighter red colour; the blood-corpuscles were moderately contracted, and began to sink in an hour and a quarter, the sinking extending to 1-16th of the volume in 18 hours; the serum was perfectly clear and colourless; the clot was of a somewhat lighter colour than that of ordinary blood, and the corpuscles were still moderately contracted.

1 volume of blood, on the addition of 0·7 of a volume of a solution of *gum arabic* (1 part in 20 of water), became very dark, and the blood-corpuscles were distended and almost spherical; they began to sink in three-quarters of an hour, and after 18 hours, had sunk to the extent of 1-40th of the volume; the blood had a blackish red colour, and was very tenacious.

100 volumes of blood mixed with an aqueous solution* of *arsenious acid*, assumed a somewhat light red colour; the blood-corpuscles were unchanged, and, after 24 hours, had sunk to the extent of 1-10th of the volume of the fluid; the serum was then red, and the blood-corpuscles were spherical and had no central shadow; several, that were lying on their edge, were reniform; all were increased in thickness.

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* [The number of volumes of the solution of arsenious acid, and its strength, are omitted by the author, apparently by an oversight.—G. E. D.]

1 volume of blood, when mixed with half its volume of extremely diluted *hydrochloric acid* (1 part of hydrochloric acid to 532 of water), became very dark; the blood-corpuscles were not much affected; they were all a little thicker than usual, and those lying on their edge were baton-shaped.

On mixing 1 volume of blood with 0·001 of a volume of *caustic ammonia,* there was scarcely any change of colour, and the blood-corpuscles were not visibly altered; after 24 hours they sank to the extent of 1-100th of the volume; the serum was then red, and the corpuscles a little distended.

The *caustic alkalies,* and several *organic acids,* as for instance, acetic acid, convert the blood into a blackish brown, thick, tolerably consistent jelly; and at the same time distend the corpuscles, and distort or destroy them.

We learn, from the observations of Harless, that the primary action of oxygen and carbonic acid on the coloured cells, is also of a mechanical nature; but this author has shown, by his variously modified experiments, that these gases likewise exert a chemical influence on every molecule of the blood; thus he found, for instance, that when we allow oxygen and carbonic acid to act alternately on the red cells, they become gradually destroyed, the destruction being usually completed after the ninth or tenth exposure to the action of the gases—an experiment which is obviously of the highest importance in connexion with the coloured cells in the circulating blood. We should therefore, at all events, be going too far if, on the above-mentioned grounds, we should ascribe the influence of oxygen or of the gases generally on the colour of the blood, solely on the changes in the form of the blood-corpuscle which they induce. The primary action of the oxygen may always be a physical one, like that of the salts; but these also act mechanically only at first; they almost all, as we have already seen, communicate a light red colour to the blood in the first moments of their action; after a longer or shorter period (varying in the case of different salts), they give a more or less dark red tint to the blood.

It is in the greater or less rapidity of the mechanical action of the salts, that the reason must be sought why a merely chemical action has been ascribed to many of them, when they were only regarded as capable of darkening the colour of the blood; as for instance, to the alkaline carbonates, (Mulder and Nasse), the salts of ammonia (Dumas), and the potash-salts, especially nitre (Hünefeld).

Nasse has shown from several carefully conducted series of experiments, that we are by no means justified in drawing any conclusions regarding the action of these substances in the circulating blood of the living body, from their action on fresh blood out of the organism. For a long time he gave to dogs and goats, food containing soda or nitre, but he either observed no action on the coagulation of the blood, or one precisely the reverse of that which he expected. I have made experiments of a similar nature with injections of solutions of *nitrate* and *bicarbonate of potash;* a solution of 30 grammes of nitrate of potash in 200 grammes of water at about 38°, was very slowly injected into the jugular vein of a somewhat overworked horse, which lost little blood by the operation. The operation of venesection was performed a quarter of an hour after the completion of the injection. The blood was rather darker than that which was discharged before the injection, and coagulated more rapidly, but formed a less dense clot and a smaller crust. In a similar manner I injected 30 grammes of bicarbonate of potash dissolved in 180 grammes of tepid water, into the jugular vein of an old but still somewhat powerful horse seventeen minutes after the completion of the injection, blood was taken from the jugular vein of the opposite side; this blood was much darker than that which escaped before the injection; the blood-corpuscles sank much more slowly, the crust was less thick, and the clot easily broken down. In the latter case the change which the blood underwent from the decomposition of the bicarbonate of potash may be easily explained: in the circulating blood, all the conditions are present which give rise to a decomposition of this salt into carbonic acid and simple carbonate of potash, namely, a high temperature, and the action of free gases; and the fluid has hence assumed the character of a blood rich in carbonic acid: the dark colour corresponds with the accumulation of carbonic acid in the blood; the neutral alkaline carbonate, rapidly as it is separated by the kidneys, had, however, here delayed the sinking of the corpuscles. The action of the free carbonic acid was also shown in the excited and, as it were, intoxicated state in which the animal remained even an hour after the injection. This condition was precisely similar to that which I have repeatedly observed in horses, after allowing them to breathe a mixture of 10% of carbonic acid and 90% of atmospheric air for from 3 to 8 minutes; the pulse increased from 36 and 40 strokes in the minute to 50 and even 54; the eyes of the animal were glistening but steady, its gait was firm, there was rumbling in the intestines, and there were eructations and a great flow of saliva.

That the *bicarbonate of potash* is converted in the blood of living animals into carbonic acid and simple carbonate or sesquicarbonate of potash, is also obvious from experiments which I have made with frogs. These animals were placed in differently saturated solutions of bicarbonate of potash or soda, and were fixed in such a manner that they could breathe freely, and that the web-membrane of one foot could, at the same time, be observed under the microscope. Within three minutes after the beginning of the experiment, the blood-corpuscles began to accumulate in the smaller capillaries of the web-membrane, while in the larger ones there was as yet no perceptible diminution of the rapidity of the circulation; in from 10 to 15 minutes, however, temporary accumulations and short stoppages were perceptible; at a still later period an oscillation began in these larger vessels, so that it was no longer possible to distinguish in which direction the current was running. As far as was possible, the blood-corpuscles of this frog were compared with those of another (not exposed to the action of a salt), whose web-membrane was simultaneously brought under another microscope of nearly the same magnifying power. Nuclei, which, as is well known, are not generally perceived in the blood-cells of frogs' blood in the act of circulation, here also could not be recognised; but although accurate measurements of the blood-cells within the web-membrane could not be made, yet a comparison of the blood-cells in the two kinds of circulating blood, showed (after a condition of stasis had commenced in the finer capillaries of the web-membrane of the frog placed in the salt), that the corpuscles of the blood in which the alkaline bicarbonate was diffused, were swollen, shortened in their long diameter, and dilated transversely. These phenomena and alterations in the dimensions of the blood-corpuscles were even more distinct in frogs which were gradually suffocated in an *atmosphere rich in carbonic acid.*

In both cases, the blood of the larger vessels and of the heart was not of a brownish red, but of a purplish colour, merging from a cherry red into an almost perfect violet; the blood-corpuscles without a decided nucleus, exhibited a central and peripheral turbidity, independent of the arrangement of the microscope; some were enlarged in diameter and volume. On the addition of bicarbonate of potash to the blood of the frog treated with carbonic acid or the alkaline bicarbonate, the fluid exchanged its purple colour for a light vermilion tint; the blood-cells were, however, so contracted that when seen under the microscope they resembled crumpled elliptic laminæ, or wrinkled and stippled shreds; their transverse diameter was so diminished that it was scarcely measurable; the nuclei were distinctly visible; they did not, however, present the ordinary form, but occurred as dark granular heaps, which distantly resembled bone-corpuscles. In both cases the serum separated very completely from the clot; both kinds of blood restored the blue to reddened litmus paper, but only that of the frog which had been exposed to the action of the salt reacted on turmeric paper. The heart of the killed or asphyxiated animals exhibited the singular phenomenon, that, when pinched with forceps, it was thrown into a state of rigid spasm, and by discharging its blood, became perfectly white. In the frogs which had breathed carbonic acid, the lungs were extraordinarily distended, bloodless, and almost colourless; while in the frogs submitted to the action of the salts, they were collapsed and of a cherry purplish colour. In a saturated solution of the alkaline bicarbonates, the frogs died in five minutes; while in a moderately diluted solution, they often remained alive for an hour and a half.

When frogs were treated in a precisely similar manner with solutions of *alkaline protocarbonates,* stoppages of the blood-current in the capillaries were also very soon observed, but no change could be perceived in the dimensions of the blood-cells (either augmentation or diminution of volume), by any possible comparative measurements; the capillaries were, however, very much filled with blood-corpuscles; the intercellular fluid appeared to be diminished, and stasis to be thus induced, precisely as occurs in the phenomena of inflammation; here also there were no nuclei to be perceived. The blood of the larger vessels had not the slightest tint of violet, but was of a pure brownish red colour; its corpuscles were, however, collapsed, in folds, strongly granular, and presented a dull granulated nucleus; on the addition of an alkaline protocarbonate, they became still more contracted, and the nuclei stood out distinctly as minute accumulations of sharply projecting granules, the entire cell having a shred-like and folded appearance, and being dotted with tolerable regularity on its border; on exposure to the air, the dark reddish brown clot assumed a light red colour. The lungs were moderately collapsed, and of a brownish red colour; the heart, on being touched, was not thrown into a state of rigid spasm, but was excited to active contractions.

In frogs narcotised with *ether,* and observed in a similar manner, some striking phenomena, very different from those hitherto mentioned, were noticed; here, during the gradual action of the ether, stoppages in the circulation of the web-membrane were remarked, but instead of an accumulation of blood in the smaller capillaries, many of them were perfectly devoid of coloured cells, so that in some nothing but a few scattered colourless corpuscles could be recognised; no blood-corpuscles any longer passed from the larger vessels into the apparently empty spaces; the diameter of the smaller capillaries was obviously so diminished that no red blood-cells could any longer enter them, and those which had been contained within them, streamed forth from their mouths, which were distinctly visible; no change could be observed in the blood-corpuscles themselves. The blood of the larger vessels was of a dark red colour, merging into violet; its corpuscles during the first few moments were normal and without a nucleus, but on exposure to the air they soon became distorted and indistinct. The lungs were usually (but not always) filled with air, and very much expanded. It is perhaps deserving of mention that after etherisation the muscles were always found in a highly relaxed condition, while after the application of carbonic acid or alkaline carbonates, there was constantly tonic spasm, and the muscles, after death, were found (as has been already mentioned) in a state of rigid contraction; if we regard this phenomenon as a consequence of irritation or paralysis of the spinal nerves, we should have observed paralysis of the vasomotor nerves of the web-membrane in rigor of the muscles, and irritation of the vasomotor nerves in paralysis of the spinal nerves.

We should scarcely have described so fully, in this place, the relations of the above-named substances in the blood of living animals, if we had not wished at the same time to use these experimental researches as a caution against the too hasty conclusions that have been drawn from the action of various chemical substances on the blood-corpuscles and other elements of the blood, with the view of elucidating pathological and pharmacological processes. If in the more recent and so called rational pharmacology, we had guarded against such crude chemical explanations, we should have avoided many errors, and kept clear of many absurd physiological fictions.

It is clear, from the preceding remarks, that many of those substances which modify the form of the blood-corpuscles, at the same time exert a chemical action on their walls; but whether they—and more especially the gases—extend their action to the contents of the blood-cells, and especially to the pigment, is a question as yet by no means satisfactorily answered. To judge from the properties of hæmatin, as described in the first volume, we should scarcely expect such an action; for we have there seen how indifferent and inaccessible hæmatin is to most chemical reagents; but, on the other hand, it is also manifest that this pigment can hardly exist in the blood-cells in the same state in which it is exhibited isolated by chemists. There is still a perfect absence of definite chemical facts to prove the almost indubitable action of oxygen on the contents of the blood-corpuscles; there are merely a few experiments made by Bruch* in support of this view, which has become more than probable from physiological grounds. The pigment itself appears to undergo changes of colour by oxygen and carbonic acid; for if strongly watered blood, in whose plasma it may be presumed that the contents of the blood-corpuscles are diffused, be shaken with carbonic acid gas, its dark colour becomes still darker in refracted (or transmitted) light; that is to say, blood which is merely watered appears, when viewed by transmitted light, of a less deep dark red colour than blood which has been similarly watered and has been impregnated with carbonic acid; we observe the opposite result on treating blood, which has been watered in this manner, with oxygen gas. This may serve to explain why the blood of the portal vein, which is richer in water than that of the other veins, is also of a darker colour.

Taking into consideration all these circumstances regarding the mechanical relations of the blood-corpuscles, it follows that a definite tint may be given to the whole blood by the action of very different influences upon the blood-cells, and that in special cases it is often very difficult to decide on which of these often opposite causes the colour of the blood in any particular case may depend.

Moreover, there are other physical relations, not directly acting on the blood-corpuscles, which may modify the colour of the whole blood. Thus we find the blood of a lighter tint when, in addition to the red cells, it contains a very large number of colourless corpuscles, or of other particles which strongly reflect light; thus Scherer showed that the addition of milk or powdered gypsum made the blood of a lighter red tint; and this is also the reason that we sometimes find the blood, in cases of pyæmia and anæmia, which abounds in colourless blood-cells, as well as the blood of confirmed drunkards, in which there are innumerable fat-globules, of a comparatively light tint.

We need hardly mention that external influences, such, for

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* Zeitschr. f. rat. Med. Bd. 1, S. 440-450, and Bd. 3, S. 308-318.

instance, as putrefaction, must act on the form of the corpuscles and give rise to chemical changes. Hence we need not wonder at meeting with blood-corpuscles of the most varied forms in the blood of dead bodies or in old exudations. It is, however, only rarely that we can draw any conclusions regarding the pre-existing disease from these forms; for they are not the direct result of a morbid process, but merely the consequence of the chemical or physical changes to which the intercellular fluid is exposed. We must not, therefore, expect any great advantage for medical diagnosis from the microscopic examination of such blood; on the one hand, because such changed forms of the corpuscles never occur in fresh blood (although they were formerly supposed to have been found in the blood in cases of typhus); and on the other, because blood obtained from the dead body always rapidly undergoes essential changes from external influences.

Having thus considered the physical characters of the blood-corpuscles, we now proceed to the investigation of their *chemical constituents.* This is a subject on which there is still much that is obscure. The microscopic examination of the blood has certainly taught us that its pigment is limited to only the coloured cells; Berzelius has further shown that in these cells there is contained an albuminous fluid, differing, however, from albumen, which he named globulin, and expressed his belief that the phosphorised fat was in all probability only contained in the blood-cells. The same chemist likewise indicated the way by which the blood-corpuscles might be separated from the intercellular fluid, or by which, at all events, they might be obtained free from the constituents of the serum, although with the loss of several of their own essential constituents. Dumas and Figuier were the first to apply this method to actual practice; and the former, by this means, was enabled to submit to an elementary analysis the dried fragments of blood-corpuscles; but, from the very nature of the case, all these investigations could lead to very few conclusions regarding the true and essential constituents of these coloured cells; for we were investigating either the blood-cells mixed with intercellular fluid, or merely the cells more or less completely freed from all soluble substances (penetrating the cell-walls). We are indebted to the ingenious and careful investigations of C. Schmidt for a more definite knowledge regarding the composition of the contents of the blood-corpuscles, and the nature of the individual substances occurring in them. We shall see that in this discovery of Schmidt's lies the nucleus of all our knowledge and theories regarding the chemico-physiological importance of the blood-cells.

Berzelius* had already found that the corpuscles were the cause of the blood's redness, and were not dissolved by salts having an alkaline basis, or by sugar, and that we had in this way a means of separating in some measure the blood-corpuscles from the intercellular fluid. Figuier† was the first who employed this means to obtain a quantitative determination of the blood-corpuscles, regarding which we shall speak more fully presently. Since, however, in attempting to separate the blood-corpuscles in this way (a solution of sulphate of soda is what is commonly used for the purpose) from the constituents of the intercellular fluid, it very soon becomes apparent that these particles, on the one hand, become agglutinated to, and stop up the filter, and on the other, that they become so changed that they pass through it. Dumas‡ recommended that oxygen should be continuously passed into the fluid lying in the filter, while, at the same time, a solution of Glauber's salts should be constantly allowed to drip into it. The blood-corpuscles obtained in this manner, and containing Glauber's salts, are dried, extracted with ether and boiling alcohol, and finally freed by boiling water from the sulphate of soda and other soluble constituents. By submitting to ultimate analysis this residue of the blood-cells freed from serum, Dumas found that both in men, dogs, and rabbits, after deducting for the ash, there was the constant ratio of from 55·1 to 55·4% of carbon, 7·1% of hydrogen, from 17·2 to 17·5% of nitrogen, and consequently from 20·2 to 20·6% of oxygen.

C. Schmidt§ exhibited in a similar manner the coagulable and insoluble parts of the blood-cells, and found their specific gravity before the abstraction of their iron to be 2·2507; but after the abstraction of the ash and iron only 1·2090. The same author found that 100 parts of this dry cell-residue contained on an average 87·59 parts of globulin and 12·41 of hæmatin. The residue, containing ash, yielded 1·179% of peroxide of iron and 0·126 of earthy phosphates.

In reference to the *cell-wall* of the red corpuscles, most French chemists, even to the most recent time, have held that this membrane was fibrin, in accordance with the old view regarding the

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* Lehrb. d. Ch. Bd. 9, S. 74. (4te Aufl.)

† Ann. de Chim. et de Phys. 3me Sér. T. 11, p. 503.

‡ Ibid. T. 17, p. 542.

§ Ann. d. Ch. u. Pharm. Bd. 61, S. 156-167.

coagulation of the blood. Denis and Lecanu have attempted to demonstrate the presence of fibrin in the blood-corpuscles by triturating them with salts, viz., nitrate of potash and chloride of sodium; Virchow, who has repeated these experiments, has however shown that the small membranes observed by these authors are nothing more than the folded and adhering walls of the blood-corpuscles, which, under the microscope, in consequence of the pressure and the crushing of the glass covering the object, often acquire the appearance of Nasse's fibrinous flakes; Virchow, however, very correctly remarked that the solubility of these membranes in a solution of nitre, and their swelling in acetic acid, by no means prove their identity with fibrin: moreover I was unable to obtain a trace of coagulable matter, or of matter precipitable by acetic acid, from the cell-membrane of the corpuscles of the blood of horses and oxen by prolonged digestion with a solution of nitre. Mulder regards the cell-wall as binoxide of protein; but the properties of the remains of the cell-walls obtained by treating blood with water by no means coincide with those of Mulder's binoxide of protein; they are far more difficult of solution in acetic acid and in the alkalies than the latter; and in these membranes I have not been able to detect any trace of sulphur, which, as is well known, is contained in binoxide of protein. Moreover, Mulder has not demonstrated the presence of this substance by direct experiments, but was merely led to this view by the following consideration: on their passage through the pulmonary capillaries, the blood-corpuscles become invested with a thicker layer of this binoxide, in consequence of which the blood-pigment appears of a lighter red colour, as if seen through ground glass, and hence the lighter red tint of arterial blood; the central depression of the coloured cells also bears out this view, since the inflammatory crust in which, as is well known, there is much binoxide of protein, has also a great tendency to exhibit a similar depression or concavity.

It is very probable that the cell-walls of the corpuscles even of the same blood have not a precisely identical composition; at all events we see that the coloured cells of the same blood are, as a general rule, very unequally acted upon by the same reagents; if, for instance, we allow water, dilute acids, ether, or dilute alkaline solutions, to act on the blood-corpuscles, we perceive that the work of destruction does not by any means proceed uniformly; thus some do not disappear even when the blood is very much diluted with water; these we consider to be the younger cells, while those which are easily destroyed are regarded as the older blood-corpuscles;

for it is believed that the capsule of the colourless corpuscles, from which the coloured cells at all events in part proceed, retains for some time its former chemical nature, even when pigment has become formed within the cell. The cell-wall, which so rapidly disappears from our sight under the microscope, is, however, actually dissolved by very few of these reagents; it only passes into a gelatinous or rather a mucus-like condition, in which its coefficient of refraction is nearly the same as that of the plasma; we arrive at this conclusion not merely from the experiment to which reference has been frequently made, by which the cell-wall may again be rendered visible either in all its integrity or at all events in fragments by solutions of salt, iodine, &c., but also from the viscidity and tenacity which are imparted to the blood by the addition of certain substances, as dilute organic acids, alkaline carbonates, iodide of potassium, hydrochlorate of ammonia, &c. If blood which has been thus modified be saturated with acids or alkalies, or if a solution of iodine or of sulphate of soda be added to it, the walls of the corpuscles again become apparent, and the blood at the same time loses its acquired viscidity. Moreover neither the intercellular fluid nor the serum is reduced by the above means to such a viscid or tenacious condition, which must therefore be dependent on the blood-corpuscles: further, mucus which had become swollen in water becomes condensed by the same means, so as to be less transparent to the unaided eye, appearing almost as if it were coagulated, and exhibiting thread-like streaks under the microscope.

The *globulin*, or coagulable matter contained in the blood-cells, as well as the *hæmatin*, has been fully considered in the first volume; we shall therefore direct our attention to the other organic substances which must be regarded as essential constituents of the coloured cells.

With regard to the *nuclei of the blood-corpuscles*, in a morphological point of view they are of very doubtful importance, since several of our first physiologists (R. Wagner amongst the number) regard the very distinct and often clearly defined nuclei of the blood-corpuscles of the amphibia as products of chemical secretion from the homogeneous cell-contents after death, while others conceive that in the discoid coloured bodies in the blood of mammalia and birds they see the nuclei or their remains. But whatever decision may be arrived at regarding the morphological existence of these elements, nothing can as yet be definitely concluded regarding their chemical nature, in the first place because we are altogether unable to isolate them for chemical examination, and secondly, because even if we recognize them as composed of a protein-compound, our knowledge of these substances is still such a vexed question, that it would be impossible to decide whether this nucleus-substance did or did not consist of one of the known and named protein-bodies.

J. Müller, and subsequently F. Simon, regarded the nucleus as fibrin in consequence of its solubility in acetic acid and in alkalies, but unfortunately these properties are not characteristic of the substance to which the term fibrin is generally applied; moreover, my observations coincide with those of Jul. Vogel, who found the nucleus very difficult of solution in acetic acid, and hence I cannot regard it as identical with fibrin. Maitland* regards the nucleus as consisting of a peculiar horn-like compound, which he named *nucleine;* Nasse very correctly remarks that the substance which Maitland obtained by washing the clot after the removal of the fibrin at the same time contains the cell-walls of the blood-corpuscles, which at all events preponderate very much over the nucleus-substance in question. Hünefeld regards the nucleus as consisting essentially of fat; that fat is abundant in the blood-cells will be immediately shown; but it is scarcely necessary to mention that in the process of exhibiting these nuclei, the fat must always become mixed with them, and consequently must always form the larger part of the object of investigation.

It has been already mentioned (see vol. i., p. 267), that a considerable part of the *fat* of the blood is accumulated in the blood-cells. Berzelius thought it probable that the so-called phosphorised fat might be chiefly contained in the blood-corpuscles. I have at all events found this view to be so far correct that the fat extracted by ether from the blood-corpuscles of the ox (obtained by means of sulphate of soda, according to Dumas's method) yielded about 22% of ash, which had an acid reaction, and consisted essentially of acid phosphate of lime. Since, however, at the present day we are justified in questioning the existence of such a phosphorised fat as was formerly supposed to exist, the idea suggests itself, that what we here meet with is the glycero-phosphoric acid discovered by Gobley in the yolk of egg (see vol. i., p. 243). In the dry blood-corpuscles of the ox I found on an average 2·249% of matter extractable by ether. We must, however, not omit to mention that the blood-cells of arterial are poorer in fat than those of

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* An Experimental Essay on the Physiology of the Blood. Edinburgh, 1838, p. 27.

venous blood; thus in the corpuscles of the arterial blood of a horse I found only about half as much fat as in those of its venous blood; in the latter the amount being 3·595%, and in the former, 1·824% of the dry prepared corpuscles.

The so-called *extractive matters* of the blood cannot be accurately indicated, since they are substances of which we have no knowledge; but this much is established from the few investigations which I have made on this subject, namely, that most of such substances pertain to the serum and not to the blood-cells. While 100 parts of the solid residue of the serum contain about 8 parts of extractive matters free from saline constituents, 100 parts of the solid residue of the cells of the same blood (calculated from the analysis of the clot) do not contain 6 parts of such substances.

In regard to the *mineral constituents* of the blood-corpuscles, very different views have been held regarding them, which are all almost equally removed from the truth; this observation, however, does not extend to the iron. It has either been believed that all the salts which we find, or presume to exist, in the serum, must also be contained in the blood-cells, or it has been assumed that at all events the soluble salts, especially the chlorides of sodium and potassium, are altogether excluded from the cells. Although neither of these views is yet generally adopted, and in the absence of all means of deciding between them, we refrain from a definite opinion, yet at all events the ideas at which we arrive from analysing the blood point only to these two modes of considering the subject. We are indebted to the unremitting investigations of C. Schmidt for a series of facts which prove that, in reality, soluble salts are also contained in the moist blood-cells, that these salts are by no means perfectly identical with those which we find in the serum, and finally, that their quantity is far smaller than it must be if the water of the blood-corpuscles contained exactly the same amount of saline matter as the water of the serum.

We need only institute a comparison between good analyses of the serum and of the clot of the same blood, and by a most simple calculation subtract the soluble salts occurring in the serum (surrounding the cells) from the sum of the soluble salts of the clot, to convince ourselves that by far less of such salts can be contained in the blood-cells than in the serum, but at the same time that these salts cannot pertain to the enclosed serum alone.

Thus, for instance, in the serum of the venous blood of a horse I found 0·835% of salts (soluble and insoluble), and in the moist clot of the same blood 0·819% of salts (including peroxide of iron);

deducting the 0·114 of peroxide of iron found in it, there remains 0·705$\frac{0}{0}$ of mineral substances; if now, we suppose by way of illustration, that the clot is so loose that it contains enclosed within it one-third of its weight of serum, then we should have to deduct 0·273 for the enclosed serum from the 0·705 of salts, and there would then remain only 0·432 of salts for the 66·667 of blood-cells (which correspond with two-thirds of the original weight of the clot); hence, in 100 parts of moist blood-cells, there would be only 0·648 of salts. If, however, we assume that the blood-corpuscles lie so closely together, that the serum which they enclose amounts to only one-fifth of the weight of the clot, then, since 16·667 parts of serum contain 0·137 of salts, there will remain only 0·568 of salts for the 83·333 parts of blood-corpuscles; that is to say, in 100 parts of blood-cells, there will be 0·681 of salts. As we shall presently show, Schmidt has now found out a method of discovering with tolerable accuracy the quantity of the serum enclosed in the clot, and hence, of calculating the mineral constituents occurring in the moist blood-cells.

Although we are able to calculate the quantity of the mineral constituents contained in the fresh blood-cells, the questions still remain to be answered whether there are certain salts which especially accumulate in the cells, and if so, which they are. These questions have also been answered by C. Schmidt; for he has discovered that the fluid of the blood-cells (that is to say, the water contained in the blood-corpuscles) contains in addition to the organic matters, a preponderance of phosphates and potash-salts; so that, consequently, the phosphate of potash and the greater part of the chloride of potassium pertain to the blood-cells, whilst the chloride of sodium, with a little chloride of potassium and phosphate of soda, is found in the plasma (serum + fibrin). In the plasma, the organic materials are combined only with soda, while in the blood-cells, the fatty acids and the globulin are combined both with potash and soda.

C. Schmidt, in analysing a specimen of blood, which contained 396·24 p. m. of blood-cells and 603·76 p. m. of intercellular fluid, found 1·353 of chloride of potassium and 0·835 of phosphate of potash in the former, while there were 3·417 parts of chloride of sodium, besides 0·267 of phosphate of soda and 0·270 of chloride of potassium in the latter.

Schmidt has examined and tabulated the relations between potassium and sodium, and between phosphoric acid and chlorine in the blood-cells and in the intercellular fluid in several of the mammalia.

The following table contains the chief results of his observations:

100 parts of inorganic matters:

Genus.	Blood-cells.		Plasma.		Blood-cells.		Plasma.	
	K	Na	K	Na	PO	Cl	PO	Cl
Man (mean of 8 exps).	40·89	9·71	5·19	37·74	17·64	21·00	6·08	40·68
Dog	6·07	36·17	3·25	39·68	22·12	24·88	6·65	37·31
Cat	7·85	35·02	5·17	37·64	13·62	27·59	7·27	41·70
Sheep	14·57	38·07	6·56	38·56	8·95	27·21	3·56	40·89
Goat	37·41	14·98	3·55	37·89	9·41	31·73	5·90	40·41

These results coincide with those of Nasse, who found the most phosphates in the blood of those animals which were distinguished for the abundance of their blood-corpuscles, namely, swine, geese, and hens; in sheep and goats, on the other hand, in whose blood he found comparatively few corpuscles, he also found the least phosphates. On another occasion, Nasse* has also expressed the opinion that the phosphates must be principally contained in the blood-corpuscles.

In man, as we see, this difference is the most obvious; in the carnivora it is most marked in the acids; and in the herbivora, in the alkalies. Schmidt adds, that the nature of the food which the animal may take, or variety of race in the case of man, exerts no influence on these relations.

Earthy phosphates, as we have already mentioned, also occur in the blood-cells, but both relatively and absolutely in far less quantity than in the intercellular fluid.

In the blood-cells of 1000 parts of blood, Schmidt found only 0·086 of the phosphates of lime and magnesia, while in the intercellular fluid he found 0·332; or in 1000 parts of blood-cells, 0·218, and in 1000 parts of intercellular fluid, 0·550 of earthy phosphates.

The *iron* of the blood pertains, as is well known, almost entirely to the hæmatin of the blood-cells; since the quantity of iron in the ash, when compared with the number of coloured blood-cells, is somewhat variable, we conclude, as has been already stated, that the quantity of hæmatin must consequently vary in the blood-cells.

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* Handwörterbuch der Physiologie. Bd. 1, S. 165.

We have seen that the blood-corpuscles obtained from the hepatic veins contain less peroxide of iron than those from the portal vein. Schmidt found an excess of iron in the blood-cells in hydræmic conditions, and hence he concludes that in these cases the blood-cells have become poorer in globulin, but not richer in hæmatin; he believes, however, that we may calculate the hæmatin from the quantity of iron found in the ash; and this conclusion certainly seems justifiable if we had to do with the pure hæmatin of the chemist, which contains 6·6% of iron; but we must take into consideration that the hæmatin, in all probability, does not start, Minerva-like, into perfect being, but that, almost to a certainty, it is gradually formed, even as it is gradually destroyed; to which it must be added that we are already acquainted with (artificially prepared) non-ferruginous hæmatin; and how, then, can we tell whether, in some organ or other, we may not discover hæmatin either altogether free from iron or, at all events, poor in that constituent?

Schmidt has convinced himself, by several series of experiments, that the clear serum of the blood of oxen, sheep, swine, horses, dogs, cats, rabbits, and hens, is perfectly devoid of iron. (Nasse had previously found this to be the case.)

In 100 parts of dry blood-corpuscles (determined according to the method of Prevost and Dumas) Schmidt found the following proportions of iron: in man, 0·4348%; in the ox, 0·509%; in the pig, 0·448%; and in the hen, 0·329%.

The *gases* of the blood, carbonic acid, nitrogen, and oxygen, are also for the most part contained in the blood-corpuscles. It has been ascertained by Davy, Nasse, Scherer, van Enschut, Magnus, and others, that the serum possesses in a far less degree than the defibrinated blood the capacity of absorbing oxygen and carbonic acid, and I have convinced myself that at least twice as much air is developed from a volume of whipped air *in vacuo* as from an equal volume of serum that has been strongly stirred or shaken with atmospheric air. Van Maack has found that a solution of hæmatin possesses a decided power of attracting oxygen; and Scherer has not only convinced himself of the accuracy of this observation, but at the same time ascertained that a little carbonic acid is developed after the absorption of the oxygen.

Davy and Berzelius believed at one time that they had convinced themselves of the presence of *free gases* in the blood, but subsequently retracted this view; after this period, the results of different experimentalists were very discordant, some being in favour of, and others opposed to the presence of gases in solution in the blood. The question was, however, decided about ten years ago, by the experiments of van Enschut, Bischoff, John Davy, and especially Magnus, which shewed that free gases are contained in solution in perfectly fresh blood, both arterial and venous; more recently, and by means of simpler experiments, Magnus * has confirmed his former observation, that, in addition to carbonic acid, both free oxygen and nitrogen occur in the blood. According to the earlier investigations of Magnus, arterial and venous blood contain nearly equal quantities of nitrogen; in the former, the oxygen is to the carbonic acid (by volumes) as 6 : 16, and in the latter as 4 : 16; hence, therefore, there is relatively more oxygen in arterial than in venous blood. His more recent experiments† determine not merely the ratio of the volumes of the gases to one another, but also to the volume of the blood; they show that at all events in the blood of calves, oxen, and horses, there are always in solution from 10 to 12·5% (by volume) of oxygen, and from 1·7 to 3·3% (by volume) of nitrogen. According to an experiment of Magendie's, venous blood contains 78, and arterial only 66% (by volume) of carbonic acid. The oxygen of the blood may also be almost entirely extracted in vacuo, as well as expelled by other gases, as for instance, hydrogen and carbonic acid; whence it is sufficiently clear that it is only mechanically absorbed in the blood, and not in a state of chemical combination. Since the blood, according to the experiments of Magnus, is capable of absorbing 1½ times its volume, or 150% of carbonic acid, it may, at first sight, appear strange that the circulating blood is not found to be more impregnated with carbonic acid, and that in respiration there is only little more oxygen absorbed than carbonic acid given off; but when we consider that in respiration the relations of the concurrent gases are altogether different from what they are in our experiments (in which we shake pure atmospheric air or pure carbonic acid with the blood), this difficulty is at once removed.

In connexion with the occurrence of free oxygen in the blood, there is an important, and indeed even yet a scarcely decided question—whether, at all events, a portion of the oxygen that finds its way through the lungs into the circulation, does not at once chemically combine, in the arterial system, with some of the constituents of the blood. Marchand attempted to decide this question by certain experiments, and Magnus by a calculation based on

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* Pogg. Ann. Bd. 36, S. 685 ff.

† Ibid. Bd. 56, S. 177-206.

established facts. Marchand believed that if blood containing no carbonic acid produces no carbonic acid by the direct influence of oxygen, the oxygen can only be mechanically absorbed: now he found, in point of fact, that fresh blood after its carbonic acid had been removed, was as incapable of developing the slightest trace of carbonic acid, when a stream of oxygen was passed through it, as the serum of the blood, egg-albumen, solutions of blood-corpuscles, &c., when similarly treated; but independently of the circumstance to which we have already referred, that van Maack and Scherer have actually observed the exhalation of carbonic acid from hæmatin after its previous absorption of oxygen, nothing more is proved by Marchand's experiment than that oxygen can be absorbed by the blood without giving rise to the formation of carbonic acid; but it is still quite possible that one or other of the constituents of the blood becomes more highly oxidised without any separation of carbonic acid, since a development of this gas does not of necessity follow every oxidation of an organic body. The mode of calculation adopted by Magnus, would be more convincing, were it not that the numbers on which it is based, rest on too uncertain determinations. If, for instance, *about* 13 Paris cubic inches of oxygen make their way into the blood of an adult man in one minute—if, further, *about* 10 pounds of blood pass through the lungs in the same interval—then, considering that *about* 11$\frac{0}{0}$ of oxygen are found in the blood of the horse, it follows that *about* half the oxygen which Magnus found in arterial blood has been absorbed from the venous blood, so that, according to this, the former would always lose about half its free oxygen in the capillaries. The preceding statement and the above-mentioned facts afford a sufficient proof that the greater part of the oxygen absorbed in the lungs, exists in a state of freedom in the blood; but it seems to us not at all indubitably established that no portion whatever of the absorbed oxygen enters into chemical combination with one or other of the constituents of the blood, even in the heart and arteries, since such a combination is believed to take place in the capillaries.

In every case the relation of the gases to the blood-corpuscles must be accurately determined by special experiments before a definite view can be formed on the subject.

Before we proceed to the more minute consideration of the intercellular fluid, we must make mention of certain morphological elements which, in addition to the coloured cells, are found suspended in the blood: these are the colourless corpuscles to which reference has already been made, and which have been termed *fibrinous flakes*. With regard to the latter, their name indicates that their discoverer, H. Nasse,[*] considers these irregular, crumpled and indented plates, which at most have a diameter of $\frac{1}{100}'''$, as a peculiar form of coagulated fibrin,—a view to which Virchow[†] has recently given in his adhesion, but which is opposed by the observations of Henle, Döderlein,[‡] and Zimmermann, who found these flakes in uncoagulated blood (both in the fresh fluid and in blood whose coagulation had been impeded by the addition of salts). Hence this substance would necessarily constitute a perfectly distinct variety of fibrin, and therefore a substance which is not fibrin: we have, however, already seen (in vol. i.) that fibrin itself has never been exhibited in a state of sufficient chemical purity to admit of our calculating a proper formula to represent its composition. But even if we allowed a wide signification to the meaning of the term fibrin, we could hardly regard this substance as fibrin after the chemical reactions which Döderlein observed these flakes to yield; for he found that they were perfectly insoluble in acetic acid (even when its action was much prolonged) and in sulphuric acid, and that they remained for weeks unchanged even after the blood had become putrid. These properties of the flakes are the very reverse of those of fibrin; and to include such a substance under the idea of fibrin, would require a greater elasticity of chemical ideas than is even now allowed. Since the relations of pavement epithelium towards acetic and sulphuric acids and towards putrefaction are precisely the same as those of these flakes, according to Döderlein's experiments, we might assent to the opinion formerly advanced by Henle, and regard the flakes as shreds of epithelium from the lining coat of the vessels, if only there was any coincidence between the forms of the two structures. At present Henle is inclined to regard the flakes as adhering membranes of destroyed blood-corpuscles, to which they certainly bear the most resemblance, as is shown by Virchow's experiments, in which he made the membranes adhere by trituration. In the copiously watered blood of the hepatic veins, which is very rich in these cell-membranes, I also found a large number of

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[*] Müller's Archiv. 1841, S. 439, and Handwörterbuch der Physiologie, Bd. 1, S. 108.

[†] Zeitschr. f. rat. Med. Bd. 5, S. 216, and Arch. f. pathol. Anat. Bd. 2, S. 596.

[‡] Henle's Handb. d. rat. Pathol. Bd. 2, S. 152.

perfectly distinct fibrinous flakes, which, like the cell-membranes, were scarcely at all acted on even by acetic acid and alkalies.

I have just read (as these sheets are passing through the press) that Bruch* believes that he has convinced himself that all the so-called fibrinous flakes are nothing more than *epithelial cells from the skin of the observer,* accidentally falling from the epidermis of the face on the preparation. The occurrence of these fibrinous flakes in most other animal fluids, their absence in the circulating blood, the adhesion of air to them, their chemical relations, the form of the horny epithelial scales, and lastly, the fact that they are found even in a single drop of water over which the head has been shaken, are sufficient grounds for the belief that the majority of the structures which have been regarded as fibrinous flakes are nothing else than dried cells of pavement epithelium; we cannot, however, explain all the formations of this kind, which we sometimes find in the blood, by assuming that they are epidermic scales. If blood has been treated with water (in the same manner in which Nasse treated his fibrin from which he saw such flakes project), we find far more of these fibrinous flakes resembling crumpled laminæ than in fresh blood, and this is especially observed when the blood of the hepatic veins is thus treated with water: these are obviously the adhering, stretched and distorted walls of the blood-corpuscles, which, as we have already indicated, resemble the epidermic scales in resisting the action of acetic acid and of not too concentrated potash ley.

According to the most recent researches, the *colourless corpuscles* are perfectly identical with the lymph- and chyle-corpuscles; indeed, notwithstanding the assertions formerly made to the contrary, no single difference can be pointed out between them and the mucus- and pus-corpuscles: we need only refer to the elaborate works and memoirs of Henle,† H. Müller,‡ and Virchow.§ The corpuscles approximate to the spherical form, and are not elastic; their investing membrane is more or less granular, and is always so viscid that the corpuscles possess a well-marked tendency to conglomerate into larger or smaller groups. In the circulating blood we see them rolling along the walls of the capillaries (while the coloured corpuscles move far more rapidly and nearer to the axis of the vessel), as may be easily perceived in the web-

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* Zeitschr. f. rat. Med. Bd. 9, S. 216—222.

† Allg. Anatomie, S. 422.

‡ Zeitschr. f. rat. Med. Bd. 3, S. 204—268.

§ Op. cit.

membrane of any frog. The contents of the colourless blood-cells consist of an albuminous solution, in which there are suspended extremely fine granules, together with a single, double, triple or multiple nucleus, which may be either smooth or granular. Water causes the corpuscles to swell, and renders the nucleus visible; the phenomenon is more marked if dilute acetic acid be used, which gradually dissolves the cell-wall, and leaves the nucleus exposed; the endosmotic action of water induces a distinct molecular motion in the granular contents of the cells.

We know far less regarding the chemical nature of the different constituents of the colourless blood-cells, than regarding that of the red corpuscles. As we must notice cells of this kind more fully in our remarks on "Pus," we shall defer for the present any further remarks on what is known on this subject.

There are other morphological elements, as fat globules, molecular fibrin, &c., which we shall notice when treating of the serum. We make no remarks on the infusoria which some have maintained that they have found in the blood, treating the subject as a long-exploded error.

The textureless fluid constituent of the blood is the intercellular fluid, which, in the circulating blood, contains the fibrin in solution, as well as the constituents of the serum; hence, we first proceed to the consideration of the *fibrin*, and the more so, since from its separation from the blood in the form of the clot, it is closely associated with the blood-corpuscles. As we have already fully noticed the chemical nature of fibrin (see vol. i, pp. 348-364), we shall here direct our remarks, for the most part, to the mechanical relations which are dependent on the spontaneous separation of the fibrin from freshly drawn blood. We shall therefore, now, principally notice the coagulation of the blood and its results—the clot and its different physical characters.

We have already (see vol. i, p. 343) referred to the views that have been advanced in reference to the cause of the spontaneous coagulation of the fibrin; we have only additionally to mention an hypothesis recently put forth by C. Schmidt,* which is essentially very similar to the opinion previously expressed by Schultz. Schmidt believes that the fibrin becomes formed and separates in the following manner: as the blood escapes from the circulation, an acid albuminate of soda which is dissolved in it, becomes disintegrated into its component parts in such a manner, that a less acid, neutral or basic albuminate of soda remains dissolved, while the other

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* Characteristik d. Cholera, u. s. w., S. 205.

atom of albumen separates under the form which we name fibrin; the fibrin subsequently contracts to the smallest possible volume, just as freshly precipitated silica, alumina, and phosphate of lime gradually contract. If we observe the separation of fibrin in threads, &c., (as described in vol. 1, p. 349), it will appear as if the analogy with hydrated alumina, &c., at all events, affords no special support for this hypothesis, which at first sight is sufficiently plausible.

The *coagulation of the blood*—the most striking phenomenon presented by fresh blood—although for a long time the subject of numerous investigations, is still involved in considerable obscurity. We now recognise fibrin as the proximate cause of the formation of the clot; we have also, in the introductory portion of this chapter, explained the process of coagulation, in so far as its external phenomena are manifested in healthy blood: but in various physiological and pathological conditions, we meet with numerous anomalies, whose study promises to elucidate the nature of this process. These anomalies, or rather fluctuations of the external phenomena, have reference partly to the duration of the individual periods of coagulation, partly to the final consistence of the clot, and partly to the manner in which the blood-corpuscles are enclosed in it. We shall have to seek for the proximate causes of these modifications, partly in the variable quantity and nature of the fibrin, and in the number and character of the blood-corpuscles, and partly also in the chemical constitution of the serum.

We shall first notice the variation in the *time of coagulating.* We much more frequently meet with cases in which the coagulation, or one or other of its stages, is delayed, than in which it is abnormally hastened. In investigating the causes of this difference, we shall at the same time become acquainted with the physiological and pathological relations under which the coagulation proceeds either more slowly or more rapidly than usual. H. Nasse must be especially mentioned, as having devoted very great attention to this department of hæmatology, and as having thrown much light upon it by his observations. We must first make mention of certain external relations, which, quite independently of the chemical nature of the blood, exert an influence on the time of coagulation. Among these, we may first notice strong agitation of the blood before, and during the process of coagulation. We find that the separation of the fibrin is more rapidly effected when the blood has been disturbed and shaken, in the same manner as in the case of saturated saline solutions, which depôsit their crystals far more rapidly when they have been stirred or agitated. The blood also coagulates rapidly in a vacuum, in consequence of the violent motion induced in the molecules of the blood, by the development of vesicles of gas and aqueous vapour; its coagulation is, however, still more rapid in the air, when the latter is strongly agitated, for here the *access of the air or oxygen* is added to the other accelerating causes. For the same reasons, the rapidity of the coagulation is increased in proportion to the slowness with which the blood flows from the vein, the length of the jet, and the width and shallowness of the vessels in which it falls. Since the blood itself contains gases, the different quantity in which they occur, must necessarily influence the period of coagulation; hence blood which is rich in carbonic acid, coagulates less rapidly than when the contrary is the case; thus, too, the longer retention of the blood in the veins, after the application of the bandage, appears to be connected with an increase of carbonic acid; at all events, we find that the blood coagulates far more slowly than usual when the bandage had been applied a long time before venesection. Moreover, when the exchange of gases is not sufficiently carried on in the lungs, the blood must become poorer in oxygen and consequently richer in carbonic acid; hence the blood coagulates very slowly in cyanosis. A similar reason may also explain, at least in part, the delay frequently noticed in the coagulation of inflammatory blood, and the less rapid coagulation of venous than arterial blood. In prolonged bleeding, the blood that flows last, is found to coagulate much more rapidly than that which escaped first, which is very probably owing to the former containing an increased quantity of oxygen, derived from the deep drawn and jerking inspirations. This mode of explanation is further confirmed by the lighter colour of this blood. The blood taken after death coagulates less rapidly, owing perhaps to its being more abundantly impregnated with carbonic acid.

Another cause which accelerates the coagulation is the *aqueous character of the blood.* According to Nasse's experiments, water accelerates the coagulation of the blood when added in small quantities, or at all events, when not exceeding twice the quantity of the blood, whilst larger quantities tend to retard coagulation. Hence we find that watery blood, as for instance, that of women or after repeated blood-lettings or other losses of the juices, and anæmic blood, generally coagulate more rapidly than blood in a normal state.

It has been long known, that certain *salts,* namely the caustic alkalies and their carbonates, have the property of retarding, or even wholly arresting, the coagulation of the blood, but the question has not yet been definitely settled in relation to other alkaline salts; for in the experiments on different salts, no attention has been paid to the degree of dilution of the saline solution, or to the quantities of the solution employed. Nasse found, however, that almost all salts accelerate coagulation when not employed in too large quantities, although they may retard it when used in very small quantities. On this account, it is far less easy than was formerly supposed to determine the connection existing between the quantity of the salts contained in the blood, and its more or less rapid coagulation in different diseases. Thus the absence of coagulability, which has occasionally been observed in the blood in typhoid and putrid conditions, has been referred to a considerable increase of the salts of the blood, or to the presence of alkaline carbonates, but this is mere opinion, unconfirmed by any experiments. All that can be asserted on this subject, therefore, is that the difference frequently observed in the period in which the blood coagulates in the same form of disease very probably depends upon the amount of the salts contained in the blood.

Viscid solutions of indifferent organic substances, such as albumen, casein, and sugar, appreciably retard the coagulation of the blood. This circumstance shows us, at all events, how many different conditions may coincide to bring about one or another of these results in reference to coagulation. But here, unfortunately, we derive only little aid from chemical analysis; for, as we have already observed, we are still in entire ignorance as to the different quantities of salts occurring in the blood during disease.

The influence of the *temperature* of the blood (as it escapes from the body) on its coagulation, has also been noticed by Nasse, but we are still ignorant how far this may effect the period of the coagulation. The difficulties of investigating more closely the causal connection of the period of coagulation and the external and internal relations of the blood, are further increased by the circumstance, that while these influences are frequently manifested in the blood, they may simultaneously neutralise one another in a greater or lesser degree.

It has likewise been conjectured that the blood when it is rich in fibrin (inflammatory blood) coagulates less rapidly than when it is deficient in that substance; but as the reverse is frequently found to occur, it appears very doubtful whether the quantity of fibrin exerts any influence whatever on the period of coagulation.

In the present state of our knowledge, in reference to the different conditions of the blood, we are alike incapable of explaining why the blood of persons killed by lightning, of those who have died from the effects of narcotic poisons or asphyxia, or from hanging, should not coagulate, whilst it coagulates very rapidly after the infliction of venomous bites, &c., and in the plague.

The *consistence of the clot* is also liable to very great variations. As the *fibrin* actually constitutes the main consolidating substance of the clot, the opinion long prevailed, and has only recently been relinquished, that the cause of this difference was to be sought in a difference in the chemical constitution of this substance; but here we have, in the first place, to take into account both the external and the internal mechanical influences, which make the clot appear at one time more dense and compact, and at another softer and more gelatinous. The vessel in which the blood coagulates, is not without its influence, for in a shallow vessel, a softer coagulum will be formed than in a high and narrow one.

We reckon, among internal mechanical causes, the relations in which the blood-corpuscles and the water stand to the quantity of the fibrin. When the *number of blood-corpuscles* is small in relation to the quantity of fibrin, its molecules approximate more closely to one another, and the coagulum is more densely compressed. But when an excess of blood-corpuscles is imbedded in fibrin which separates gelatinously, the latter may remain imperfectly contracted during its further consolidation, and thus give rise to a highly friable clot. As the lower part of the clot, moreover, contains the greater number of blood-corpuscles, it is evident that this portion will continue to be softer and looser in texture, whilst the upper part becomes more dense and connected. On this account, we find that the clot in the blood of plethoric persons is large and soft, whilst in that of chlorotic patients it is small and firm.

The fact that too large a quantity of *water* diminishes the consistence of the clot, has chiefly been proved by Nasse, both by direct experiments and by observations on morbid watery blood. It would appear as if the molecules, which are separated in a gelatinous form at the commencement of coagulation, could not be brought into sufficiently close contact with one another to admit of their firm contraction; and hence, the clot may in such cases retain too much serum, which will render it soft and friable. This excess of water may also contribute to produce that greater softness which we observe in the clot of young animals, and may be the cause of the softness noticed in the clot after frequent blood-lettings. As, however, exceptions to these observations sometimes present themselves, we must presume that other influences frequently supervene which counteract the effect of the water. It follows, therefore, that we are unable to draw any conclusions regarding the relations of weight between the serum and the actual coagulum, from the relative volumes of the clot and of the serum; since we should have to consider in such an estimate, whether the fibrin in its condensation had completely pressed out the serum.

Henle further draws attention to a mechanical influence, which may give rise to the formation of a soft and very diffluent coagulum, at least in some few cases; for when the blood slowly flows in *separate drops*, each drop forms, in a certain degree, a coagulum which does not combine with the other drops to form a homogeneous and connected mass. Henle assigns this as the cause of the incoagulable character of the menstrual blood; but Schmidt's and my own observations (to which we shall refer in a future page) have shown that this blood does not contain any fibrin.

The *gases* contained in the blood appear to exert some influence on the consistence of the clot; for whilst a light red, highly oxygenous blood yields a dense, elastic coagulum, the clot appears to be soft in all conditions in which the blood is rich in carbonic acid; this is especially manifested in asphyxia—a condition in which it has been asserted that the blood exhibits no capacity for coagulation.

It is not impossible that *other constituents of the blood* may influence the consistence of the clot; at all events we find in artificial experiments with salts which retard coagulation, that a soft and frequently even a mere gelatinous coagulum is formed. The soft, friable, and often tar-like consistence of the clot in putrid diseases, may therefore be owing to free alkalies or their carbonates.

We are unable, at the present time, to determine whether the differences manifested in the physical character of the clot, depend upon differences in the *chemical constitution* of the fibrin. Some observers have conjectured that there are different kinds of fibrin; we have already spoken of parafibrin, &c., but no differences in the nature of fibrin admit of being chemically demonstrated; nor are we logically compelled to assume the existence of such differences, since the different forms under which the fibrin coagulates, may possibly depend upon the action of certain chemical relations, of which we are still ignorant. When we remember that ordinary albumen may form either a gelatinous and milky, or a flocculent, or a membranous coagulum, without having experienced any alteration in its elementary composition, we cannot admit the necessity of regarding the buffy fibrin of the inflammatory coat as chemically different from that which is separated, in a crumbling or flocculent form from tar-like blood.

The *form of the coagulum* mainly depends upon the relations of the blood-corpuscles to which we have already referred. We have seen that, under certain conditions, the blood-corpuscles are disposed to approximate to one another by their flat sides, thus assuming a cylindrical form, and that in this manner they more readily displace the column of fluid which supported them, and sink more rapidly; whilst those cells which are of a jagged, twisted, or spherically distended form, impede such a cohesion, and give rise to a more prolonged suspension of the molecules. The different forms of the clot must, therefore, obviously depend upon the different *sinking capacity of the blood-corpuscles.*

The rapidity or slowness with which the *fibrin* is separated and consolidated, exerts in the same manner a determinate influence on the form of the clot. The differences existing in these proximate causes prove how difficult it is to explain in a special case the remote causes which may give rise to any definite form of the clot. If we here take into account the two proximate causes of difference, namely, the time of coagulation of the fibrin and the sinking capacity of the blood-corpuscles, we find two cases especially which give rise to a different conformation of the clot, namely, *rapid coagulation of the fibrin with little tendency of the corpuscles to cohere,* and *slow coagulation of the fibrin with rapid sinking of the corpuscles.*

Henle first drew attention to the fact that the red sediments of blood-corpuscles, which are often deposited from the blood when there is a dense clot, are owing to the fibrin coagulating and becoming contracted before the corpuscles had assumed the roll-like or nummular form; on the contraction of the gelatinised fibrin, a large number of the loosely connected or wholly isolated blood-corpuscles are again expressed, by which means the serum is for a time rendered turbid and red, until they afterwards separate into the above mentioned sediment, which readily admits of being again disturbed. Zimmermann, who confirmed this view of Henle's by a microscopical examination of the red deposit, found, moreover, that besides this sediment there was always present a small but very compact clot, which proves that the coagulation of the fibrin acted an important part in this phenomenon.

We far more frequently observe the converse relations in diseased, and even sometimes in healthy blood—that is to say, the corpuscles have a strongly marked sinking capacity, whilst the fibrin coagulates slowly. We must here bear in mind that extreme cases are of the rarest occurrence, and that both properties are wholly relative; for in the one case the fibrin may contract as usual within an average time of coagulation, while the corpuscles sink more rapidly; and in the other case, the corpuscles may sink with their ordinary velocity only, while the fibrin, on the contrary, coagulates very slowly. The result will be much the same in both cases. The influence of these two causes may be perceived even in the normal clot, for here we find that the lower part of the clot is always darker and softer than the upper one; this depends, certainly, only in part upon the circumstance that there are more blood-corpuscles which have already sunk in the lower than in the upper portion, for the light colour of the upper part depends on the one hand upon the access of oxygen, and on the other upon the larger number of colourless blood-corpuscles, which, although they combine in groups, owing to their viscidity, are not so very closely in contact in consequence of their spherical forms, and do not, from their lightness, sink as rapidly as the red corpuscles. When the red corpuscles of fresh blood have sunk in some degree before the fibrin becomes gelatinised, the fibrin coagulating in the uppermost stratum of fluid is unable to enclose any red corpuscles, and consequently forms a colourless crust upon the subsequently deposited clot. As this crust encloses only few foreign elements, the fibrin of which it consists contracts more closely than that which is beneath it, and in which the blood-corpuscles are embedded. This crust will therefore not only present a smaller diameter than the red clot, but it must also, from its contiguity, cause an extension of the margins of the latter, while it gives rise to a concavity of the clot. This concave and generally very compact and yellowish white *buffy coat* is of most common occurrence. It is principally found to occur in the venous blood of horses and in inflamed blood, and sometimes also in human blood, if drawn during the process of digestion. A plane or convex buffy coat is also observed in many morbid conditions; in these cases it is soft, and of a greyish white colour; and it is not improbable that this character depends no less upon an excess of colourless blood-cells and vesicles of fat in the crust, than upon the slight contractility of the fibrin.

Although this mode of explaining the formation of a fibrinous or buffy coat scarcely needs any additional grounds for its establishment, Müller, H. Nasse, and Henle have confirmed it by special experiments; for they formed an artificial buffy coat from blood that was not buffed, by employing means either for accelerating the sinking of the blood-cells, or for retarding the coagulation of the fibrin. Nasse found, moreover, on comparing the blood of different animals, and by closely examining diseased buffy blood, that the time in which the blood-corpuscles sink bears an inverse relation to that in which the fibrin coagulates. Nasse and others have, however, also frequently seen cases in which rapidly coagulating blood formed a buffy coat; these instances do not, however, present any exception to the rule, since they only show that the sinking of the corpuscles has proceeded more rapidly than the coagulation of the fibrin.

We must not omit all mention of certain relations which, although they do not constitute the sole conditions necessary for the formation of a buffy coat, may contribute simultaneously with other causes towards its production. Among these we must first instance *the form of the vessel* in which the blood is suffered to coagulate. In a high narrow vessel, the blood-corpuscles are sooner removed from the level of the fluid than in a wide and shallow one, and thus leave a part of the fibrin to coagulate without them; on this account, strongly inflamed blood is often found to yield no buffy coat in a flat vessel, whilst, on the contrary, blood which is considered to be of a non-inflammatory character exhibits a buffy coat if received in a narrow cylinder.

The *number of the corpuscles* is another cause which contributes to the formation of this coat. When the number of corpuscles is small and their sinking capacity is considerable, a buffy coat will more readily be formed than where the blood-corpuscles are present in large numbers. On this account a buffy coat is more frequently formed after a second or third, than after the first venesection The same cause explains its more frequent occurrence in the blood of anæmic and pregnant females, than in that of healthy and non-pregnant women.

It was formerly regarded as a well-established view, that the formation of this coat was owing to an *excess of fibrin;* and as the increase of the fibrin was in general proportional to the progress of inflammation, it was also termed the inflammatory crust. It cannot be denied that the quantity of the fibrin exerts some influence on the thickness of the buffy coat, but it can never constitute the sole cause; for we frequently observe inflammatory blood, which is very rich in fibrin, form no crust, whilst, as we have already noticed, blood that is poor in fibrin may in many chronic affections present a crust of this nature.

We have, therefore, to revert to many different proximate or remote mechanical and chemical causes for an explanation of the configuration of the clot in any special case. The observations regarding the mechanical relations of the clot are only important in a semeiotic point of view in special cases; they are of no service in the establishment of artificial families or groups of diseases.

Before we pass to the further consideration of the substances actually dissolved in the intercellular fluid, we have to notice some bodies which remain suspended in the blood, or more correctly speaking, in the *serum*, after the separation of the fibrin and the blood-corpuscles.

Hewson and Thomson are of opinion that they have found a milky *turbidity of the serum* in blood taken some hours after a meal; but I have never observed anything of this kind either in carnivorous or herbivorous animals, whose blood I have examined at different periods after the administration of food. In a similar manner the serum acquires, according to Hewson and Magendie, a milky appearance after prolonged fasting. Nasse found that the serum of the blood of pregnant women was in most cases milky; very frequently, but not invariably, we observe that in drunkards the serum presents an opalescent, almost milky turbidity. This turbid appearance is generally due to the presence of suspended *fat*, which may easily be detected by microscopical examination or by shaking the serum with ether.

Zimmermann has drawn attention to a kind of turbid serum, which he has found in the blood in inflammatory conditions. This turbidity depends upon the presence of very small dark particles, or molecular granules; and hence he was induced to assume the existence of a special molecular fibrin, while Scherer, on the contrary, who has noticed similar instances of turbidity, inclines rather to the opinion that these granules are separated albumen. My own observations on the turbidity arising from molecular granules lead me to concur in the latter view; for I found that the turbidity disappeared on the addition of neutral alkaline salts, when the serum exhibited only a faint alkaline reaction; and hence we must assume, with Scherer, that a portion of the alkali is by some means removed from the albuminate of soda in the blood, and that a portion of the *albumen* has been separated in a finely granular form, after the removal of the alkali which had been combined with it. (See vol. i., p. 333.)

In some cases the turbidity of the serum depends upon the presence of suspended *colourless blood-cells*, as both Pieschel and myself have observed in the blood of dogs affected with the mange.

If it be admitted that the physical relations of morbid blood, as it flows fresh from the vein, is a subject of considerable importance, the character of the *blood in the dead body*, in respect to the mode of its coagulation and its colour and consistence, cannot be devoid of interest to the pathologist. However strongly we may protest against the doctrine of crases, which is based on such investigations, as a perversion of the so-called pathologico-anatomical tendency, we cannot withhold our testimony to the value of the labours of such inquirers as Rokitansky and Engel. The connexions which Engel has ingeniously established between the nature of the blood in the dead body and its imbibition in the tissues, its accumulation in separate organs, and the character it impresses on the individual tissues, as well as regarding the nature and extent of the preceding exudations or transudations, show that we are justified in looking for a rich accession to our scientific knowledge from a more exact chemical investigation of this subject. Unfortunately, however, no chemist has as yet been inclined to direct his attention to this subject. Hence we do not deem it altogether superfluous to follow the arrangement of Rokitansky and Engel, and to consider the different kinds of blood in the dead body with reference to the above physical properties, classifying them in the six following groups:—

1. One kind of blood found in the dead body is distinguished by its thick fluid character, its reddish brown colour, and its coagulability; and is probably for the most part characteristic of a certain group of diseases, since it is only met with in the bodies of persons who have died from violent inflammations (with the exception of inflammatory affections of the brain and the spinal cord). Blood of this kind becomes bright red on exposure to the air, and coagulates only in the larger vessels; in the capillaries and the smaller vessels it retains its thin fluid nature, and the coagula which occur in the heart and in the larger arteries, as well as the larger veins, are almost always compact, and of a dark brownish

red colour. The thickness of this blood is the cause why it is less readily infiltrated into the tissues than other blood. It is moreover worthy of notice, that fibrinous coagula never occur simultaneously with these clots in the heart and the larger vessels, for when they are present, they are found in the vessels of moderate calibre, but never in the capillaries.

2. The blood in acute diseases of the spinal cord and of the brain is found to be thickly fluid, of a dirty brownish red colour, uncoagulated, and devoid of fibrinous coagula.

3. A thick, uncoagulated, and not coagulable blue and blackish red blood, which, under certain favourable conditions, sometimes deposits fibrinous coagula in the heart and the larger vessels, is certainly not characteristic of merely one form of admixture of the blood; for blood of this kind is found in the body after diseases which reciprocally exclude one another, as, for instance, after plethora (depending upon heart diseases), typhus, acute tuberculosis, cholera, and poisonings with narcotics and lead, and after sudden and profuse sweats or diarrhœas.

4. A pale, or vermilion-red, uncoagulable, thin fluid blood, which, notwithstanding its fluidity, does not readily infiltrate the tissues, but which often deposits a considerable quantity of fibrinous coagula in the larger vessels, does not belong to any special admixture of the blood, since it is met with after the most varied conditions of disease, when the blood has acquired a watery character; as, for instance, after frequent venesections, hæmorrhages, considerable exudations, long-continued diarrhœa and sweats; and in the anæmia following typhus and the acute exanthemata, as well as in senile atrophy.

5. A thin bluish black, uncoagulable blood, which is distributed in large quantities from the great to the smallest vessels, which easily infiltrates into the different tissues, and which never exhibits any separation of fibrinous coagula, is found in valvular anomalies of the heart.

An accurate analysis of this variety of blood, compared with the composition of the blood in the living body, during the existence of the different conditions arising from mechanical difficulty and obstruction of the function of respiration, as, for instance, plethora, hæmorrhoidal affections, dropsy, &c., would undoubtedly yield the most valuable aid towards the explanation of the mechanical and chemical metamorphosis of matter in the animal body.

6. Finally, there is a kind of blood found in the body after death,

which is thinly fluid, uncoagulable, and of a dirty brownish colour, does not deposit fibrinous coagula, is easily infiltrated into the tissues, but is generally found to occur in inconsiderable quantities in the heart and the large vessels, while it is accumulated in abundance in the capillaries. This condition is observed in true decompositions of the blood, as for instance, in pyæmia, puerperal fever, scurvy, &c.

We are still in the dark as to the direct origin of those polypous coagula of fibrin which are deposited from uncoagulable blood containing but little fibrin; and all that we know in reference to the subject is, that the retarded circulation induced shortly before death by mechanical obstruction as well as by debility, is favourable to the deposition of these masses—and hence their occurrence after a protracted death-struggle. The formation of the purely local fibrinous coagula observed in aneurisms, obliteration of the veins, phlebitis, &c., may be explained in a similar manner.

We now pass to the consideration of the actually *dissolved chemical constituents of the serum;* amongst which we must first direct our attention to *albumen.* As we have already fully considered this substance in its various relations to other protein-bodies, and to the other constituents of the blood (see vol. i., p. 342) it only remains for us to notice one or two additional points.

The question has often been raised, whether the albumen in different vessels, under different physiological relations, and in different pathological conditions, is always identical. Physiological, no less than logical grounds, warrant us in answering this question in the negative, although chemistry affords but little aid in determining the point. We have already seen (in vol i., p. 332) that many modifications in the properties of albumen depend upon the different quantity of alkali or salts which it contains, while the organic group of atoms in the albumen has always remained the same. Differences in the albumen, depending upon an augmentation or diminution of the quantity of alkali, that is to say, neutral, basic, and acid albuminates of soda, occur even in the normal condition, as for instance, in the blood of different vessels. The solution of neutral albuminate of soda becomes turbid on the addition of water. This combination occurs not only in morbid blood (as Scherer was the first to show), but also in the blood of different vessels, as also in the blood of the splenic vein; and here, independently of the other metamorphoses experienced by the blood in the spleen, a portion of the basic albuminate of soda is saturated by the free acid which we find in the parenchyma of that organ, and the neutral compound is thus formed. The serum of the portal blood appears, moreover, less turbid on the addition of water than that of the splenic vein ; while that of the hepatic veins exhibits great turbidity on the addition of water; and here the albumen of the portal vein, probably, loses a portion of the alkali which is applied to the formation of the bile.

In accordance with Scherer's view, we must regard the different form in which the albumen coagulates, as dependent upon the different quantity of alkali which it contains (see vol. i. p. 333) ; but still we often observe, that where the alkaline fluid has been neutralised or faintly acidified, in order to induce such a complete deposition of the albumen as may be necessary for its perfect filtration, the albumen of one blood collects less easily in flakes, and is less readily filtered, than that of another. Thus, I constantly found that the albumen of the blood of the hepatic veins only accumulated in masses very slowly, often not till it had been boiled for hours, whilst that of the portal and other veins, as well as that of the arteries, very readily coagulated on boiling after the addition of an acid, and that it rapidly sank, leaving a clear supernatant fluid.

Since, as we have already observed, ordinary chemical investigations, and more especially elementary analyses, still fail to throw much light on the enquiry into the essential differences in the protein-bodies, C. Schmidt* has conceived the happy idea of bringing substances that are readily capable of fermentation or decomposition into contact with the constituents of the blood under favouring conditions, and thus employing sugar, urea, amygdalin, asparagin, &c., as tests for the presence of certain modifications of albumen; as yet, however, the only results at which he has arrived, are that the blood-cells of a healthy individual (but not the intercellular fluid) contain one substance which yields sugar-ferment as the product of its spontaneous decomposition, and another which similarly yields urea-ferment. In diseases, as for instance in cholera, one or the other of these fermenting bodies is increased to a great degree.

We have already (in vol. i., pp. 249 and 279) fully considered the fats of the serum, and we need, therefore, here simply remark that only a small quantity of free fat occurs in the serum, while saponified fat is always present in large quantities, as well as the crystallisable lipoids, cholesterin, and serolin. It cannot be shown, with certainty, that the serum contains any phosphorised fats. We shall perceive from special numerical results, that the quantity of the fat,

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* Characteristik der Cholera, S. 57—68.

and also the kinds of fat occurring in the different veins and under different physiological relations, present great variety. The fat of the serum as compared with that of the blood-corpuscles, may be regarded as more readily crystallizable, and less tenacious and colourless, but far inferior in respect to quantity. The difference between the quantity of fat contained in the intercellular fluid and that of the blood-corpuscles is obvious from the above review of the quantitative distribution of the different constituents in the corpuscles and the intercellular fluid. We would only observe, therefore, that the considerable quantity of fat which is mixed with the fibrin, has very frequently been regarded as peculiar to that constituent. Virchow[*] found from 2·50 to 2·76% of fat which could be extracted with alcohol and ether in human venous fibrin, Schmid[†] from 4·21 to 5·04% in the fibrin of the jugular vein of horses, and from 7·37 to 8·72% in that of the portal vein, whilst I found 2·154 in the buffy coat of the venous blood of the horse, and 2·168% in the arterial blood of the same animal.

It is certainly of some importance in a physiological point of view to decide whether the fat which can be extracted from this substance is of a peculiar kind, and exists in chemical combination with it, or whether it is only incidentally mixed with this substance, that is to say, from purely mechanical causes. It has been usual to follow the views of Berzelius in this respect, and to regard this fat as peculiar to the fibrin, and as distinguished from other fats of the blood by the amount of nitrogen it contains; but a more attentive consideration of the mode in which the fibrin is exhibited, leads us to doubt the correctness of this opinion. We have here only to consider the mode of preparation of the fibrin, and the admixtures which it always contains; the fibrin in its spontaneous coagulation must necessarily draw down and enclose particles only suspended in the blood, and in addition to these and the blood-corpuscles, occasionally very minute fat-vesicles, and always colourless blood-cells. When the fibrin is obtained by washing the clot, the granular contents of many coloured blood-cells, which mainly consist of fat, remain in the fibrin together with the cell-walls. We have already shown in an earlier part of this work (see vol. i. page 352) that many colourless blood-cells are mixed with the fibrin, and it must further be observed, that they contain, absolutely and relatively, more fat than the coloured cells. We do not call in question the possibility that acid salts of the

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[*] Zeitschr. f. rat. Med. Bd. 4, S. 266—293.

[†] Heller's Arch. Bd. 4, S. 322.

fatty acids in the serum (enclosed in the clot) may be rendered insoluble by strong dilution with water. There are at all events, a number of possible sources to which the fibrin-fat may and indeed must in part be referred. It is only necessary therefore, for the determination of this question, to ascertain whether this fibrin-fat differs specifically from the fats associated with the other constituents of the blood. Such, however, does not seem to be the case, for as far as my own and Virchow's enquiries extend, the fibrin only contains fats which belong to some one or other of the blood-constituents. Virchow found a considerable quantity of acid phosphate of lime in the ash of this fat; the other reactions of the fat seemed also to confirm the presence of glycero-phosphate of lime, which, as we have seen, is peculiar to the coloured blood-cells. There is also an acid ammonia-soap contained in the fibrin-fat, which may possibly have been conveyed to it by the serum. We know so little of the non-saponifiable fats, that they cannot aid us in deciding this question either negatively or affirmatively. Virchow could not detect cholesterin in the fibrin of man, but I have demonstrated its presence in the fibrin of horses by the micrometrical measurements of its angles. It might indeed also be derived from the serum. It follows from the above observations, that we are not as yet justified in ascribing special fats to the fibrin. We might perhaps be disposed to attach some weight, as far as this question is concerned, to Virchow's observation of an acid reaction of the fat of the fibrin, but independently of the fact that the fat of the coloured blood-cells exhibits a similar reaction, there are several grounds for explaining this phenomenon. In the first place, these fats, as they contain the salts of the fatty acids, must assume an acid reaction whenever the ether which is employed, is not entirely pure, (free from acetic acid, aldehydic acid, &c.), and from several investigations in relation to this subject, I am disposed to think, that the metamorphosis of the ether into acids, by the action of animal substances, is considerably promoted by prolonged digestion. On the other hand, we can the less wonder at the acid reaction of these fats, since the salts of the fatty acids precipitated with the fibrin by water, are acid salts, from which on fusion volatile and acidly reacting fatty acids are separated from their combinations with bases. Thus, for instance, we constantly find volatile fatty acids in these fats (both in those of the fibrin and of the blood-corpuscles), as for instance, acetic acid, which may be produced by the metamorphosis of the ether, and at least *one* acid, which, when treated with baryta, yields a salt which crystallises into beautiful laminæ, and which undoubtedly belongs to the group of the true volatile fatty acids.

With regard to the *extractive matters* of the serum, it is better to pass them over in perfect silence, than to collect the fragmentary and inconclusive facts regarding them at present in our possession, (see vol. i. page 320.) From the physiology of the metamorphoses going on in the blood, we should be led to suppose that the extractive matters are far more abundant in the intercellular fluid than in the blood-cells, and this view is confirmed by direct experiment; for, as is obvious from what has been already stated regarding the composition of the blood, these substances occur more abundantly, both relatively and absolutely, in the serum than in the cells.

A number of substances were formerly included and concealed among these extractive matters of the blood, and especially of the serum, which have either lately been discovered or which we have not yet succeeded in finding. First amongst these we must place *sugar*. This has very recently been proved by C. Schmidt* to be an integral constituent of the normal blood of cattle, dogs, cats, and diseased and healthy men. It has been already mentioned, that in consequence of Bernard's discovery of sugar in the liver, I sought for this substance in the blood of the portal and hepatic veins, and found 10 or 12 times as much in the latter as in the former, in which the quantity was very small.

The method of determining the amount of sugar in the blood is very simple: freshly drawn and defibrinated blood is gradually treated with 8 or 10 times its volume of alcohol, the mixture being thoroughly shaken; the coagulum is washed with hot alcohol, and the alcohol of the filtered fluid driven off; the residue is further concentrated, and then extracted with stronger alcohol, whereby the greater portion of the salts is separated; a part of the alcoholic fluid is now treated with an alcoholic solution of potash, by which the potash-and-sugar compound and a little extractive matter are precipitated; the precipitated flakes become caked together on the filter, from the action of the air; we then dissolve them in water, and can determine the sugar qualitatively by Trommer's, and quantitatively by Fehling's test. Another part of the alcoholic solution (from which the greater part of the salts has been removed in the above-described manner) may be evaporated, dissolved in water, and treated with a little yeast; and the quantity of sugar can then be calculated from the carbonic acid which is evolved. (See vol. i., p. 288.)

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* Characteristik der Cholera, u. s. w. S. 161—164.

Other substances occurring in the serum of normal blood are *urea,* (see vol. i. page 164), *uric acid,* (vol. i. page 217), and *hippuric acid.* The latter has been found by Verdeil and Dollfuss* at Giessen, in the blood of oxen. That *creatine* and *creatinine* occur in the blood, has certainly not yet been proved by direct investigation, but from the simultaneous occurrence of these two substances in the muscular juice and in the urine, we are justified in concluding that they exist there.

Whether *biliary matters,* to wit, the *biliary acids,* occur preformed in normal blood, we have not at present the means of deciding (as has been already mentioned in page 81) ; on theoretical grounds, we should, however, regard their presence as improbable.

We are still perfectly in the dark regarding the *pigments* of normal serum (see vol. i. page 299).

The faint yellow colour which is peculiar to normal serum, certainly does not depend on bile-pigment; at all events, we cannot exhibit the well-known and striking reactions of cholepyrrhin with the extracts of the serum. In diseases, the serum often assumes an intense yellow colour, with or without simultaneous turbidity; this depends either on bile-pigment, which is recognisable in the blood, not merely in icterus, but sometimes also in cases of pneumonia, or on an augmentation of the above-mentioned little understood serum-pigment, (which is also most frequently observable in inflammatory processes), or lastly, on suspended blood-corpuscles. Schultz is of opinion, that hæmatin may also occur in solution in the serum, if the contents of the blood-cells become diffused in it, in consequence of a deficiency of salts in the blood. Such cases must, however, be very rare.

We have little to add to what has been already stated, regarding the *salts* peculiar to the serum (see vol. i., p. 431, and p. 189 of this volume). While phosphates and potash-salts predominate in the blood-corpuscles, we find a preponderating quantity of *soda-salts,* and especially of the *chloride of sodium,* in the serum; on an average we also find far more salts in the serum than in the blood-cells (after deducting the iron). *Alkaline sulphates* and *carbonates* belong also principally to the intercellular fluid.

Before concluding our remarks on the qualitative examination of the blood, we must mention the persistent *odour* which is peculiar to that fluid, and which is particularly evolved on mixing blood with a larger quantity of sulphuric acid, as for instance, 1

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* Compt. rend. T. 30, p. 510 et 657—660.

volume of blood with 1½ of acid. Barruel* believed that he had ascertained that the blood of every kind of animal possesses its own peculiar odorous principle, and stands in a definite relation with the odour of the cutaneous and pulmonary transpiration. These and several other opinions of Barruel, having reference to medico-legal investigation, have not been altogether confirmed. They have been submitted to a very careful experimental criticism by Schmidt,† who found that the peculiar odour was evolved in an unmistakeable manner by the blood of the goat, the sheep, and the cat, while the odour which was developed from the blood of other animals did not possess a distinctly specific character.

According to Barruel, the odorous principle of the blood is more distinct in the male than in the female sex in every species of animal; as, moreover, it may be developed from the serum, it would appear to pertain to that portion of the blood. Further, the manner in which this odour is developed, indicates that we are here dealing with volatile acids which belong, or at all events are closely allied to the butyric acid group.

The general remarks which we have made regarding the analysis of the animal fluids, especially apply to the *analysis of the blood.* The shortest possible critical review of the different modes that have been adopted for analysing the blood, will fully confirm the truth of those observations.

One of the most important deficiencies in the analysis is obviously connected with the circumstance that the primary and most important physiological question, namely, the quantitative relation between the fresh *blood-corpuscles* (with their moist contents) and the plasma belonging to them, cannot be answered in the present state of analytical chemistry. We must hence rest satisfied with determining, at all events approximatively, the solid, coagulable and insoluble constituents of the blood-corpuscles; we say approximately, for even the methods of determining the insoluble matters of the blood-cells have in part only a relative value; their quantity is usually not directly found, but calculated from several determinations; moreover, the originator of every indirect method of determining the blood-corpuscles must admit that his method never can give a perfectly correct result, even for hypothetically dry blood-cells, since it is impossible to declare, by any of these indirect methods, how much of the constituents of the serum

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* Ann. d'Hygiène publique. No. 6. 1829.

† Diagnostik verdächtiger Flecke in Criminalfällen. Mitau u. Leipzig, 1848, S. 19.

enclosed in the clot, is still adhering to the blood-corpuscles, and must accordingly be deducted. The worst deficiency in all blood-analyses however is, that the errors are not constant, even when the same method is employed; that is to say, the acknowledged error in every analytical method is of variable magnitude, so that even the comparative blood-analyses made according to one and the same method—a procedure on which the French chemists lay such stress—have only a very subordinate value for physiology and pathology, and the conclusions drawn from them can only be received with the most extreme caution. We must confess with sorrow, that even at the present day the analysis of the blood must be ranked amongst the most uncertain and untrustworthy investigations in the whole department of analytical chemistry. Hence, the attempt which has been recently made (by Hinterberger under the superintendence of v. Gorup-Besanez*) to prove experimentally the comparative certainty of the different methods of analysing the blood, is the more praiseworthy; it is only in this way that we shall attain to what at present seems in some measure impossible. We ought not, however, to expect that chemistry at its beginning should equally distribute its full light over a field on which scarcely a glimmer of twilight has fallen during preceding centuries of investigation.

Most of the experimenters who have made large series of blood-analyses, namely, Andral and Gavarret,† Becquerel and Rodier,‡ and Popp,§ have scarcely at all deviated from the method by which Prevost and Dumas‖ determined the dry blood-corpuscles. This method consisted, essentially, in separately weighing the serum and the clot, after the perfect contraction of the latter, in order to determine the ratio in which they stood to each other; the solid residue of the serum was then determined, as also was that of the clot; on deducting the fibrin, which had been otherwise determined, from the solid residue of the clot, we obtain the number which expresses the sum of the dry blood-corpuscles and of the solid residue of the serum still enclosed in the clot. It is in the accurate determination of the amount of this serum that our most able experimentalists have broken down. Since the amount of

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* Arch. f. phys. Heilk. Bd. 8, S. 603—618.

† Ann. de Chim. et de Phys. T. 55, p. 227.

‡ Gaz. méd. de Paris, 1844. No. 47, p. 751.

§ Untersuchungen über die Beschaffenheit des menschl. Blutes in verschiedenen Krankheiten. Leipzig, 1845, S. 68.

‖ Ann. de Chim. et de Phys. T. 23, pp. 56—75.

water in the clot probably stands in a near ratio to that of the serum, Prevost and Dumas unquestionably believed that they were most nearly approximating to the true ratio, when they regarded all the water found in the clot as pertaining to the serum, and calculated accordingly the amount of the solid constituents of the serum contained in the dry clot, the amount of fibrin being previously deducted.

Since the whole of this calculation depends on a mere simple proportion it would be quite superfluous to enter into further particulars regarding it.

I cannot imagine, as C. Schmidt appears to assume, that Prevost and Dumas actually believed that all the water of the clot depended only on the serum, but I think it more than probable that they took the view which we have already described. Since the quantity of the serum enclosed in the clot could not be absolutely determined, and as there was no available means of estimating it, the only alternatives that remained for them were, either to calculate all the water of the clot (after deducting the fibrin) as belonging to the blood-corpuscles alone, or as belonging to the serum alone; and they chose the latter. Neither they nor any of their followers have supposed that either of these views was not decidedly erroneous; they, as a matter of course, chose that which obviously led to the smaller error. Von Bibra seems, therefore, to have fallen into a mistake, in believing that by disregarding the serum contained in the clot, he could diminish the error of these chemists.

The modifications of this method which other experimentalists, namely Becquerel and Rodier, and Popp, have adopted, all retain the same error to which we directed attention in speaking of the plan originally made use of by Prevost and Dumas; the former determined the solid residue of the defibrinated blood, and deducted from this the solid residue of the serum which they calculated from the amount of water (the solid residue being determined from a separate analysis of the serum). Popp analysed the serum that separated from defibrinated blood, and then the cruor which was formed under this serum. These modifications, although not essential, are undoubted improvements on the original method; for it would be folly to attempt the impossibility of thoroughly drying the clot, as it is obtained from the coagulation of the blood; if, however, we take a portion of the clot for the determination of the solid residue, we must at all events adopt the caution of analysing a vertical section of it, since the corpuscles are very unequally distributed in the clot from above downwards. In many cases it is better to separate the serum from the cruor, according to Popp's method, than from the clot according to the method of the French chemists. This separation of the serum from the sunk corpuscles by any method is however, in most cases, the most uncertain part of the analysis; for in drawing or pouring off the fluid portion from the clot, it rarely happens that the serum is obtained perfectly free from blood-corpuscles, or the clot perfectly free from serum, independently of the quantity which is enclosed.

Although, however, all authors have been compelled to admit that this mode of determining the dry corpuscles can have no absolute value, it has been generally regarded as perfectly available and sufficient for comparative analyses of the blood; but we must remember with what very different power the fibrin contracts in the clot in different diseases; a very dense clot will enclose far less serum than a very loose gelatinous one; and we do not take into account, that sediments of blood-corpuscles often occur external to the clot: further the serum obtained from the blood-corpuscles occurs in no definite proportion, since the quantity of serum remaining mixed with the corpuscles is less dependent on the manipulation of the operator than on accident.

Simon* struck upon a method of finding the quantity of the blood-corpuscles directly, which however is altogether wanting in accuracy. He coagulated whipped blood by the application of heat, stirring or shaking it the whole time, and then extracting the coagulum with ether and boiling alcohol: he thought that boiling alcohol left the albumen of the serum in a state of purity, and dissolved the constituents of the blood-corpuscles together with the salts and extractive matters of the serum; after the evaporation of the alcoholic solutions, the residue was extracted with cold aqueous spirit which, as Simon appeared to believe, left undissolved all the constituents of the blood-corpuscles, while it dissolved the non-coagulable matters of the serum. This method presents so many imperfections that one only wonders how Simon's blood-analyses should coincide so tolerably well with those of other experimenters. In illustration of the utter unfitness of this method it may suffice to mention, that two analyses of one and the same blood, made according to Simon's directions, would never by any chance coincide. This method, in consequence of its minuteness of detail, has never been adopted in large series of blood-analyses.

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* Med. Chem. Bd. 2, S. 83 [or English Translation, vol. 1, p. 175].

Scherer[*] has in many respects improved the analysis of the blood, and his method is the most correct that has yet been suggested, although it presents the same prominent deficiency as the others, namely, the mere determination of those constituents of the blood-corpuscles which are coagulable and insoluble in water, together with the uncertainty attaching to the absolute value in consequence of the impossibility of estimating the serum that is actually enclosed. Thus, Scherer does not compare the solid residues of the serum and of the defibrinated blood, but the quantities of the coagulable constituents of both fluids, in order to find the number of dry blood-corpuscles, and calculates the salts, fats, and extractive matters independently. From the comparative investigations of Hinterberger, it appears that Scherer's method yields the smallest number for the blood-corpuscles, and the reason of this is easily seen; for the dry corpuscles, in Scherer's analyses, are deprived not only of all their soluble constituents, but also of an undetermined quantity of earthy phosphates, by the acetic acid employed in the coagulation, and in addition to this, a little pigment sometimes remains in solution in the fluid, notwithstanding the boiling and neutralisation, and there is then so much lost in the calculation of the blood-corpuscles. The principal reason may, after all, lie, as v. Gorup-Besanez and Hinterberger have suggested, in the manner in which Scherer obtains the defibrinated blood, which is as follows: he applies pressure to the clot, and mixes the fluid which escapes with the serum—a method of procedure by which a greater or lesser number of corpuscles, or at all events of their remains, must invariably be retained in the fibrin, and thus be lost in the determination of the mass of the dry blood-cells.

We now arrive at a method which appears to avoid the errors of those we have previously described, and to separate the whole of the serum from the corpuscles. It is based on the property (mentioned in p. 183) which a solution of Glauber's salts possesses of rendering the blood-corpuscles capable of being retained on a filter. It was first applied by Figuier, and subsequently improved by Dumas, and more recently by Höfle[†]. Defibrinated blood is treated with eight times its volume of a concentrated solution of Glauber's salts and filtered, the residue on the filter is rinsed with the same solution (Dumas simultaneously conducts a stream of oxygen through the mass lying on the filter), and finally the mass of blood-cells retained on the filter is either directly coagulated

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[*] Otto's Beitrag z. d. Analysen gesunden Bluts. Würzburg, 1848.

[†] Chemie u. Mikrosk. am Krankenbette. S. 132.

with hot water (Figuier) or is first washed off the filter in tepid water, and then coagulated by boiling. Practicable and accurate as this proceeding appears at first sight to be in theory, it is not to be depended upon in practice. Notwithstanding the precautionary rules recommended by Dumas, some of the blood-corpuscles almost always pass through the filter, and this is the more likely to occur, the more rapidly the corpuscles adhere in dark red masses to it; but even when the filtered fluid appears only little coloured, we can always detect plenty of corpuscles in it with the microscope, or at all events perceive the deposition of a red sediment; the fluid often passes so slowly through the filter, that the latter becomes completely blocked up by the more or less altered blood-corpuscles. This method of procedure is very often inapplicable to diseased blood, either from its corpuscles passing as readily through the filter after the addition of sulphate of soda as before, (Didiot and Dujardin*) or because the serum is so viscid and almost gelatinous, that it will not pass through the filter. In a very small number of cases this difficulty may be got over by substituting a solution of sugar for one of sulphate of soda (Poggiale†). This is, however, the most important question—Is all the serum actually separated in this manner? If this were the case, this method might at all events be used as a check to other methods, as for instance to Scherer's, and we should thus probably be able to discover a coefficient for the error (consequent on the serum retained in the clot) which is unavoidable in the preceding methods; but unfortunately this is not the case, for the corpuscles collected on the filter are by no means free from serum after two or three washings with a solution of Glauber's salts, as Höfle believes; for the fluid running off the corpuscles even after six or eight washings, is not free from the constituents of the serum, (if indeed so many washings do not cause the disintegration of the corpuscles or the clogging up of the filter;) this is the reason why, as Gorup and Hinterberger found, this method yields more dry blood-cells than any other, nothwithstanding the above mentioned loss of corpuscles and their constituents, (which, when the globulin of the blood-cells is imperfectly coagulated, remain dissolved with the sulphate of soda, especially if a little acid has not been added to the fluid to be coagulated). This excess of blood-cells becomes more intelligible when we have convinced ourselves (as I have often done) that clear blood-serum becomes strongly turbid by a saturated

* Compt. rend. T. 23, p. 227.

† Ibid. T. 25, pp. 198—201.

solution of pure sulphate of soda. Hence, notwithstanding the most careful washing, substances are added by the serum to the corpuscles. Moreover, in examining the ash of the blood-cells determined by Höfle's method, Hinterberger found a large amount of sulphates. This, however, I have never observed when the coagulum was properly washed with hot water. But, on carefully considering the application of this method, we find that in theory also there are certain objections to it. Thus, if we wash the blood-corpuscles with a fluid which leaves the walls of the cells uninjured, the permeability of the walls is not by that means impeded. We know that the soluble salts of the blood-cells permeate the cell-walls; hence it would be very remarkable if the soluble coagulable protein-bodies of the cell-contents could not also partially penetrate the cell-membranes after the removal of all the serum, in accordance with the laws of endosmosis. Moreover the substance retained in the blood-corpuscles (as C. Schmidt has shown) loses potash by its solution in water and subsequent coagulation, and besides this also organic matter; so that this method, even if all the serum could be removed from the blood-corpuscles, would prove insufficient to determine the solid constituents of the blood-cells.

C. Schmidt* is the first who has attempted the solution of the problem, to determine the relation of the moist blood-cells to the intercellular fluid. His mode of proceeding is not based, as might be supposed, on the direct determination of the dry blood-corpuscles by means of sulphate of soda, but, on the contrary, on the original method of Prevost and Dumas. Since the investigations of the most accurate analysts show that the solid constituents of the serum stand in a constant relation to those of the clot, that is to say, since the richness of the clot in solid constituents is proportional to the degree of concentration of the serum, it follows that the number representing the dry blood-corpuscles, calculated according to Prevost and Dumas' method, must also stand in a constant relation to the fresh corpuscles existing in the blood. It thus became necessary to discover the constant factor by which we might calculate the blood-cells (in the morphological sense) from the hypothetical dry blood-corpuscles found by Prevost and Dumas' method. Schmidt has found that this coefficient is equal to 4, so that we have only to multiply the hypothetical dry blood-corpuscles by 4, in order to obtain the number representing the moist blood-cells. Schmidt's experiments show that a number, larger or smaller by 0·3 than 4·0, fails

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* Charakteristik der Cholera. S. 3—19.

to give the correct relation. It was chiefly by the three following methods that Schmidt was enabled to determine this factor :—

1. He determined, by micrometrical measurement, the diminution which the red blood-cells undergo on drying. If they are dried under circumstances which admit of an uniform evaporation of water in all directions, Schmidt finds that they undergo a constant diminution of volume, amounting to 68 or 69% of that of the fresh cells ; hence the latter contain about 68 or 69 parts of water to 32 or 31 of solid substances, or nearly four times as much of solid constituents as is dissolved in the plasma.

2. After Schmidt had convinced himself that the quantities of serum expressed from the clot at different times had the same density and the same composition, he investigated by the microscope the volumetric relation existing between the blood-cells and the intercellular substance (fibrin + serum) in the clot in its most contracted state ; and ascertained that in 100 volumes of clot, there are at the most 20 volumes of intercellular substance, or one-fifth of the whole volume ; if, therefore, the four-fifths of the volume of the blood-corpuscles in the clot be compared with the volume of the whole blood (clot + serum), we find that the blood must contain at least 40%, by volume, of fresh cells ; Schmidt moreover found, in further comparisons of this kind, that, as a general rule, the blood contains a larger volume of blood-cells, and that it may rise to 53 or 54% of the whole volume.

3. The third equation of condition which Schmidt applied to the determination of this coefficient, depends on the comparison of the unequally divided mineral constituents in the clot and serum. It has been already fully demonstrated that potash-salts and phosphates predominate in the blood-cells—a point on which any one may easily convince himself by comparing an accurately made ash-analysis of the clot or of the cruor (if the fibrin has been removed) with that of the corresponding serum. Since, unfortunately, the serum is never entirely free from phosphates and potash-salts, while the blood-corpuscles are never entirely free from alkaline chlorides and soda-salts (in the analyses made by Schmidt, and in accordance with his method), this might appear to be the best check on the coefficient established by Schmidt ; but unfortunately it cannot be used to ascertain, in a special case, whether Schmidt's calculation of the relation of the cells to the intercellular fluid be correct. If there were a substance to be detected in the serum, so peculiar, and so easily separable and determinable quantitatively, by chemical means, as the hæmatin in the blood-corpuscles, then from the

analysis of the clot, and from the quantity of this substance peculiar to the serum, it would be very easy to calculate how much serum (which must obviously also have been analysed) was inclosed in the clot; if then we deduct the other constituents pertaining to the serum (as determined by the analysis of it), from the quantity of similar substances and the fibrin found in the clot, we should at once obtain, by the simplest calculation, the quantity and the composition of the blood-corpuscles contained in 100 or 1000 parts of blood. If this were the case, the problem would be completely solved, but, unfortunately, neither in the pre-formed sulphates nor in the organic matters can we find a substance which is entirely excluded from the blood-cells. Hence, in all probability, we must for ever rest satisfied with Schmidt's coefficient, as affording the closest approximation; but if other parts of the blood-analysis were equally accurate, this coefficient would always afford highly correct results. Physiology, and especially physiological chemistry, are indebted for the most brilliant results to this ingenious combination of Schmidt's.

Schmidt's method of calculation in analysing the blood is very easy of comprehension: we have the analyses of the clot and of the serum, and the proportion (calculated from these data) of the constituents of the whole blood: if we multiply by four the number of the dry blood-corpuscles calculated by Prevost and Dumas' method, we obtain the quantity of fresh blood-cells, and hence their ratio to the intercellular fluid. We now deduct, from the analysis of the whole blood, the constituents belonging to the quantity of intercellular fluid, and the remainder represents all the substances belonging only to the blood-corpuscles.

No one has yet attempted a quantitative determination of the *colourless blood-cells;* it is probable that we shall never arrive at more than an average estimate of them.

We have already spoken (in vol. i., p. 356) of the quantitative determination of the *fibrin,* and pointed out that it is not to be relied upon. We will here only add a few words regarding the results of Hinterberger's experiments, which show that we always obtain less fibrin by whipping the blood than by washing the clot. He is of opinion that the evaporation of the water occurring during the coagulation of the blood, may be one of the causes of this difference; considering, however, the comparatively small quantity of fibrin in the blood, the error arising from this cause would be infinitesimally small, and in the best analyses of the blood would be overbalanced by other errors of observation; thus, one of the first rules of analytical chemistry is, that liquid and volatile fluids which are to be submitted to quantitative analysis should never be allowed to stand, if it can be avoided, even to be weighed in open vessels; hence a specimen of blood intended for quantitative analysis should never be allowed to coagulate in an open vessel, and then perhaps to stand for 24 hours. But in following this analytical rule, direct experiments show us that we obtain less fibrin from the whipped blood than from washing the clot. We have already shown, in the first volume, that even the fibrin obtained by whipping, since it can be only imperfectly washed, is never pure fibrin; and this is far more the case with fibrin obtained from the clot; while a little blood-pigment always remains in the former, the latter contains colourless corpuscles and the walls as well as the granular contents of the coloured cells. The colourless cells and the walls of the coloured cells may often occur in such quantities as entirely to falsify the number representing the fibrin: indeed, in the blood of the hepatic veins we have already become acquainted with a case in which scarcely any fibrin occurs, and where it was merely the cell-membranes of the blood-corpuscles that were mistaken for fibrin. The greater number of the fine flakes which in whipped blood penetrate the linen filter, are cell-membranes of this sort, the flakes of fibrin being in fact comparatively few; the pseudofibrin of the blood of the hepatic veins passes almost entirely through the linen filter. Hence, in an analysis, we have the two alternatives, either of losing some of the fibrin or of simultaneously including in the calculation both colourless blood-corpuscles and cell-walls; hence more fibrin will invariably be obtained from coagulated blood, in which these elements are firmly enclosed by the fibrin, than from whipped blood, whose fibrin (if no water has been added) had been separated by a linen filter. Moreover, linen filters are not to be trusted for a quantitative analysis; for they either allow a number of minute flakes of fibrin to pass through them (whether the fibrin be obtained by whipping, or by kneading and pressing the clot), or they become invested with a fine viscid crust of cell-walls, by which even the widest meshes of the linen become clogged up. Hence, in making as accurate an analysis of the blood as possible, a linen filter should be altogether avoided for the quantitative determination of any of the constituents, and we then find that the fibrin obtained from the clot does not exceed that which is obtained by whipping the blood; and further, that the experiments instituted by Marechal, and more recently repeated by

Corne,* on the influence of motion on the diminution of the fibrin, and the deductions they have drawn from them, are entirely dependent on errors in their mode of analysis. It is certainly impossible altogether to avoid these errors; for if we carefully collect all the insoluble substances passing through the linen filter, the number which we obtain for the fibrin is too high. The following is, we believe, the best, although it is by no means a perfect method of collecting all the insoluble matter which collectively goes under the name of fibrin: whipt blood must be strongly watered, and the flakes allowed to deposit themselves, (this deposition is, however, often very imperfect;) the fluid, as far as it has become clear, is to be drawn off, and the turbid residue, with the coarser clots, to be repeatedly shaken with water, and the clear fluid to be removed till water ceases to be at all coloured by it; afterwards, if it be possible, a paper filter must be used, through which the fine flakes cannot penetrate, in place of a linen one; previously, however, heating the fluid with an equal volume of spirit. (When the fluid has once become colourless, no more coagulable substance is generally found in the fibrin.) The fibrin may then be tolerably easily collected on the filter, and it should afterwards be washed with boiling spirit. We cannot even in this way accurately determine the fibrin; but we know what we have to deal with, and that if we always determine the fibrin in excess, it is far less dependent on pure casualties than if we had used linen filters, or had partially watered the blood; in one case any calculation is impossible, in the other we know that there is always an excess of fibrin and a slight loss of blood-corpuscles. Our knowledge of the error leads us to hope that we may subsequently learn to avoid it: accuracy and patience are indeed indispensable in this mode of determining the fibrin. Moreover, in this somewhat circumstantial operation, the blood does not readily undergo putrefaction, in conquence of the frequency with which the water is changed.

For the method of determining the *albumen* in the serum, we must refer to the observations already made in p. 339 of the first volume. In regard to the special application of those remarks to the analysis of the blood, we need only add that it is always important, besides determining the albumen in the serum, to determine also the coagulable matter contained in the clot, or the clot when free from fibrin, or in the defibrinated blood, as a controlling check which is indispensible in blood-analyses; so as in some degree to combine the methods of Becquerel and Rodier, or of

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* Compt. rend. T. 30, p. 110.

Popp, with that of Scherer. Hinterberger found that the amount of albumen, when determined according to Becquerel and Rodier (by extraction of the solid residue of the serum with various indifferent solvents), was always somewhat larger than when determined by Scherer's method; this is, however, not merely the case with the serum, but also, in a still higher degree, with the cruor when free from fibrin (the blood-corpuscles + the enclosed serum); that is to say, here also the substance obtained by coagulation through the aid of acids, amounts to less than the residue which we obtain after treating the solid constituents of the cruor with ether, alcohol, and water. This result, which can be observed in any analysis of the blood, partly depends upon the circumstance that when the coagulation is effected by the aid of acids, they extract from the coagulable matter a small quantity of earths which would naturally remain in the substance, if treated only with indifferent menstrua; but partly also on this, that, by the treatment with such menstrua certain alkaline salts, and probably also organic matters, are extracted from the residue, which, in the coagulation, retain in solution a certain quantity of albuminous substances from the fluid, so that this portion is abstracted from the coagulation.

A. Becquerel* has recently availed himself of Biot's discovery of the rotatory power which dissolved albumen exerts on polarized light, in order to determine the quantity of albumen dissolved in the serum, as Bouchardat had previously attempted to do. We cannot give a minute description of the instrument in this place, but we may observe that it enables us to measure the rotation which a pencil of light undergoes to the left hand in consequence of the albumen contained in the fluid. According to Biot's formula, the rotatory power of albumen is 27° 36′; in Becquerel's apparatus, the *albuminimeter*, each minute of deviation which the pencil of light undergoes, corresponds to 0·18 of a gramme of albumen in the solution inclosed in the apparatus, and hence every degree corresponds to 10·8 grammes. Becquerel has found, by repeated observations, that there is a perfect coincidence between this physical and the chemical analysis; but this is a subject requiring further investigation; in the first place, because, according to Becquerel's admission, even the chemical mode of determining the albumen does not give strictly accurate results; and secondly, because the serum always contains traces of sugar, which may, to a certain degree, modify the amount of the deviation.

The determination of the *salts* of the serum and of the cruor

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* Compt. rend. T. 29, p. 625.

is best accomplished by carbonising the solid residue of each, and then adopting the modification of Rose's method, which is described in p. 407 of the first volume. The salts can then be analysed in accordance with the rules recently laid down by Rose, whose labours have gone far to bring this department of analytical chemistry to a state of perfection.

The quantitative determination of the *fats* in the blood, as in other animal substances, is associated with difficulties which often cannot be entirely overcome. As a matter of course, we only employ for this purpose the solid residue, after thorough drying at 120°. The best method of procedure is to introduce into a small digesting flask the dry substance which is to be employed for the determination of the fat, while we determine its weight, as in elementary analyses, by re-weighing. A small digesting flask is necessary for this purpose, since it is only thus that we can boil the substance with ether, and pour off the ethereal fatty solution without loss of fat. The ethereal solution is then to be evaporated from a small glass cup or basin with a very high border, because the fat very readily creeps up to the edges, and thus necessarily occasions loss. Moreover, the ether must be perfectly pure,—as free as possible from water, alcohol, and free acid. The evaporation of the ether must be accomplished without boiling; and the fatty residue, like all other residues, be dried at 120°.

Pure ether extracts only the neutral fats and the free fatty acids, and not the *alkaline salts of the fatty acids;* the latter must be extracted with absolute alcohol, to which about one-tenth of its volume of ether has been added. The determination of the soaps is always uncertain, because, as a general rule, we do not obtain them in sufficiently large quantities to separate the non-fatty substances which almost invariably intermingle with them.

To calculate the *extractive matters* by deducting from 100 parts of the fluid the sum of the constituents obtained by direct analysis, is a procedure by no means to be recommended; for by such a course we lose one of the most important means of checking or controlling the whole analysis. After the removal of the fats from the solid residue which we are going to analyse, the extractive matters, that is to say, the alcoholic, spirituous, and watery extracts, must be dried, weighed, and finally incinerated, in order that the ashes (after their determination) may be abstracted from the organic matter; it is only in this manner that we can hope to attach any scientific value to these extractive matters, which, in a physiological point of view, are doubtless of much importance.

We certainly cannot apply all the controlling checks which we have here described in every analysis of the blood; but as the little regarded rule holds good (see p. 3 of this volume), that the smallest possible quantities give the most accurate results for each individual determination, by no means so large a quantity of material is requisite for a good analysis of the blood, as we are commonly in the habit of supposing necessary. It is only for analyses of the ash that larger quantities are required, and even here the accuracy attainable in inorganic analysis is now so great, that a comparatively small quantity suffices.

Sugar and *urea* may sometimes be determined quantitatively in the blood; on these points it is sufficient to refer to what has been already stated in p. 91 of the present volume, and pp. 159 and 164 of vol. i.

In relation to the *determination of the specific gravity*, we shall more fully notice this subject in the chapter on "the urine," when we shall examine the different methods which have been proposed for this purpose. With regard to the blood, we need only remark that it is very often almost impossible to determine the density of the cruor free from fibrin, and of the defibrinated blood, in consequence of the viscidity of this fluid, and of the air-bubbles suspended in the blood, and, in particular, adhering to the vessel.

A full consideration of all the circumstances and accidents appertaining to chemical analysis, must shake our confidence in the relative accuracy of those analyses of the blood of which we are at present in possession, and we might even hesitate in ascribing any degree of value to the deductions and hypotheses which have incautiously been drawn from them. Then, moreover, it must be remembered that in many diseases in which the admixture of the blood is most altered, good analyses of blood cannot, from considerations of humanity, be adequately prosecuted, and that in reporting such analyses, we have generally been contented with a vague and abstract diagnosis, although the course of the individual morbid process is of the highest importance in a scientific point of view: hence no great weight can be attached to a humoral pathology which is based on such slender supports. If, finally, we consider that in all kinds of analysed blood, the result refers only to the greater or lesser fluctuations in the relations of the main constituents of the blood, and not to a new alteration, admixture, or decomposition of that fluid, and since these relations have not yet been adequately elucidated in a chemical point of view, we can only wonder that it should ever have been supposed that such scanty materials could aid us in obtaining any insight into the obscure mysteries of morbid processes. We will not deny that thanks are due to those who have prosecuted the most comprehensive investigations with minute carefulness and disinterested labour; but we should be untrue to the cause of science, did we fail to set forth the real character of these results.

We have already attempted, at the beginning of this chapter (see page 160), to give a general view of the *quantitative composition of the blood;* and we will now proceed to consider the varying proportions of the individual constituents under different physiological and pathological conditions.

The ratio of the *blood-cells* (in the morphological sense) to the intercellular fluid, appears to undergo very slight fluctuations in the normal state when the physiological conditions are analogous. In an adult healthy *man*, we find on an average 512 parts of moist blood-corpuscles in 1000 parts of blood; the fluctuations do not exceed a difference of more than 40 in either extreme, so that while 472 would be a very low number, 552 would be a very high one for the proportion of cells in the blood of a man.

According to the above described method, the dry blood-corpuscles found by Prevost and Dumas, amounted to 129 p.m., by Lecanu* to 132·5, by Andral and Gavarret† to 127, by Richardson‡ to 134·8, by Becquerel and Rodier§ to 141·1, by Nasse‖ to 116·5, by Popp¶ to 120, and by Scherer** to only 112.

It is scarcely necessary to observe that no conclusion regarding the proportion of the cells to the plasma can be drawn from the proportion of the serum to the clot: as we have already seen in the preceding remarks the sinking capacity of the blood-corpuscles on the one hand, and the contractility of the fibrin on the other, present such variations that we may readily comprehend how one voluminous clot may contain very few blood-corpuscles, whilst another which is less voluminous may contain a proportionally larger number of cells.

In the blood of *women* we find on an average fewer cells than in that of men; their number is still more decreased during

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* Etudes chimiques sur le sang humain. Paris, 1837.

† Recherches sur les modifications de quelques principes de sang, &c. Paris, 1842.

‡ Thomson's Record of General Science, vol. iv., pp. 116—135.

§ Recherches sur la composition du sang, &c. Paris, 1844.

‖ Op. cit.

¶ Op. cit.

** Op. cit.

pregnancy, before the period of menstruation, and after its entire cessation towards the close of the climacteric period.

We are especially indebted for the determination of these relations to Becquerel and Rodier, who give 127·2 as the mean number for the corpuscles of the blood of women. Nasse, in his experiments on the blood of animals, has found the same differences in the different sexes.

Prevost and Dumas*, Berthold† and Simon‡ have shown by direct investigations, as might indeed be conjectured, that the number of blood-corpuscles varies in the *blood of different animals;* and more recently the same subject has been fully considered, especially by Nasse§, but likewise by Andral, Gavarret, and Delafond.‖ According to these researches, it would appear that the cold-blooded animals contain far fewer blood-cells than those having warm-blood, birds on an average more than mammalia, but carnivorous not more than herbivorous animals. The blood of the pig contained relatively the largest number of cells.

Nasse found in the blood of the pig 145·5 p.m. of dry blood-corpuscles, in that of the hen 144·6, of the goose 121·4, of the dog 123·8, of the ox 121·8, of the horse 117·1, of the cat 113·4, of the calf 102·5, of the sheep 92·4, and in that of the goat only 86·0 p.m. The results obtained by the other enquirers can only be compared with one another, but do not admit of a comparison with those of others. It is worthy of notice that Prevost and Dumas found the corpuscles in the blood of the land-tortoise to be very abundant, and even relatively more numerous than in the blood of the duck, the raven, and some of the mammalia. The correctness of these numbers ought to be investigated, since land-tortoises bear great affinity in an anatomical point of view to birds, whilst sea-tortoises stand in a nearer relation to fishes.

It may be shown with tolerable accuracy, that the quantity of the corpuscles is not the same in *the blood of all the vessels;* for when, for instance, the urinary secretion is very active, the venous blood in the kidneys will contain relatively more corpuscles than the arterial blood of those organs. In consequence of the essential

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* Bibliothèque nouvelle, T. 4, p. 125.

† Beiträge zur Zootomie, u. s. w. Göttingen, 1831.

‡ Lehrb. d. Ch. Bd. 2, S. 235 [or vol. i., p. 339 of the English translation].

§ Handwörterbuch der Physiologie. Bd. 1, S. 138; and Journ. f. prakt. Ch. Bd. 28, S. 146.

‖ Ann. de Chim. et de Ph. 3me Sér. T. 5, p. 304.

differences which take place in the blood-corpuscles of the spleen, the venous blood of this organ is found to differ from the arterial, not only qualitatively, but also quantitatively, in reference to the blood-cells. We learn from the investigations of Mayen, Hering, and Nasse, that the arterial blood contains fewer blood-corpuscles than the venous. Schmid found a much smaller number in the portal blood than in that of the jugular veins; I found a much larger quantity in the blood of the hepatic veins than in that of the portal vein, and even more than in that of the jugular veins, the vena cava, and the splenic vein.

In the blood of the hepatic veins of a horse which had been fed four hours before death, I found 743 p.m. of moist blood-cells, whilst there were only 592 in the blood of the external jugular vein of the same animal, only 664 in that of the vena cava, 573 in that of the portal vein, and only 322 in that of the splenic vein.

My own experiments, as well as analogous physiological observations, concur in showing that *scanty nutrition* and *prolonged abstinence from all food* diminish the number of the blood-corpuscles.

From what has been already said in reference to the function of the liver (see page 101), and the influence of fat on the formation of cells (vol. i. page 266), we need not wonder that Popp should have found an augmentation of the number of the blood-corpuscles, and more especially of the colourless ones, *after the prolonged use of cod-liver oil.*

We should naturally expect that repeated venesections would occasion a diminution in the number of blood-corpuscles; and Andral and Gavarret, Simon, Becquerel and Rodier, Zimmermann, Popp and Nasse, have shown by direct experiments that this is the case. Although the correctness of these views has been proved by all the inquiries instituted on the subject, no average proportion has as yet been established between the diminution of the blood-corpuscles and the quantity of the blood abstracted, or the number of times venesection has been performed.

We cannot hope to discover a definite proportion between the decrease of the blood-cells and the abstraction of blood, until we can accurately determine the individual magnitudes of all the coincident momenta. It is not difficult to perceive, that for the present, no such determination can be arrived at; for the intercellular fluid will in one case (as for instance, from deficient nutrition in already depressed and reduced organisms) be less rapidly regenerated than in another, and on this account there will be a less marked difference between the blood-cells and the plasma; whilst, on the other hand, the blood-cells may, under favourable conditions, be more rapidly reproduced, and in that case also, the relation between the plasma and the cells would be less unequal. Finally, it may happen that the blood-cells are more rapidly destroyed in one organism than in another, and hence the difficulty of determining these physiologically important relations is increased. Moreover, experiments of this kind have usually been instituted during the manifestation of morbid processes whose various characters and modes of development have not been taken into consideration.

Since the coloured blood-cells, as we shall subsequently show, are produced from colourless cells, it is not surprising that after repeated or very copious venesections (Remak) the ratio of the colourless cells to the coloured ones should be considerably increased, or, at all events, that the former should be less diminished in number than the latter.

It has even been found, that during different periods of one and the same blood-letting, the relation between the blood-cells and the plasma is not always constant. Becquerel and Rodier, who specially investigated this subject, did not arrive at any definite numerical relations. In the great majority of cases, the corpuscles were diminished in the blood which flowed last, but sometimes they were increased. No light, however, can be thrown on this subject as long as we remain in ignorance of the physical relations existing between the relative amounts of the blood and of the other juices of the animal body.

It will be long before we can hope to establish any fixed relations of comparison between definite physiological processes and the increase or diminution of the number of blood-corpuscles in morbid blood. We constantly find the blood-cells augmented in plethora, in the earlier stages of heart-disease, in spinal irritation (Popp), and in cholera (C. Schmidt). It may be readily conceived that a diminution in their numbers is of more frequent occurrence, especially in those anæmic conditions which generally supervene upon profuse diarrhœas, prolonged suppurations, slow intermittent fever, typhus, copious exudations, exuberant morbid growths, cerebral affections, chronic metallic poisonings, and other severe diseases; in short, in all cases where the formation of the blood is less than its consumption. In chlorosis, which properly speaking is only an anæmic condition, and which, from our ignorance of its immediate cause, has been termed spontaneous anæmia, the coloured blood-cells are extraordinarily diminished, although Becquerel and Rodier state that they have observed two cases of this disease in which the chlorotic blood was rich in corpuscles. During the first eight or ten days of typhus, the blood-corpuscles are always increased; but subsequently to that period, at least until the twenty-first day, their number is considerably diminished. In other diseases, we are unable to trace any very perceptible fluctuations in the number of the corpuscles; and hence the results of most experimentalists do not coincide very closely. Becquerel and Rodier, as well as Popp, agree however in asserting that the number of blood-corpuscles is diminished in violent inflammations, pneumonia, and acute articular rheumatism.

In *chlorosis,* the amount of the dry blood-corpuscles has been found to sink to 80, and even as low as to 46·2 p.m. In *spinal irritation,* Popp found 120·5 p.m. as the lowest number, and 140·5 p.m. as the maximum (his mean normal number being 120); in *plethora* he found the corpuscles much less increased than in spinal irritation. Schmidt, who found 513 moist blood-cells in normal male blood, saw the number rise to 559 in cholera; in the blood of women, (where the mean number for the corpuscles is about 400 p.m. according to him,) the number has risen to 464. The bare results of the analyses cannot attain any physiological value until we are able to determine the conditions in which this augmentation of the corpuscles is absolute, or in which it is merely relative; and for the present we can only hazard a conjecture in reference to this question. In cholera the apparent augmentation is only relative; for the admirable investigations of Schmidt and others on the blood in cholera show that in this disease water and salts are the principal constituents which are lost, that the serum is consequently thickened, but diminished in volume, and that its ratio to the blood-cells is therefore also diminished. Moreover, according to Schmidt's calculation, a number of corpuscles are destroyed in cholera, so that the blood of a healthy individual contains absolutely more blood-cells than that of a cholera patient.

In the earliest stage (within the first week) of typhus, as well as in plethora and spinal irritation, we are inclined to believe that there is an absolute increase of cells; at all events, no separation of serum, or of any of its constituents, is ever observed in these conditions.

We forbear entering any further into the detail of the observations made on the proportion of the corpuscles to the intercellular fluid in diseases, since they have not led to such complete and available results as to justify us in more fully noticing this subject without some deeper insight into the individual pathological processes.

Very little is known regarding the alterations which the *chemical composition of the blood-corpuscles* undergoes under different physiological and pathological relations, since no light has hitherto been thrown upon their morphological condition; enquirers having limited themselves to an attempt to determine the frequently mentioned dry blood-corpuscles, without reference to the water appertaining to them, or to the soluble constituents which they may contain. If we were to attempt to calculate these relations from the older analyses, we should readily be led into error, even if our calculations were not wholly impracticable; since all the relations cannot be taken into account when we draw deductions from an investigation which has been entered upon from wholly different points of view. We regard a mere re-calculation of the analyses as of little or no use, unless they are tested by others conducted by better methods, and prosecuted from a different point of view. Science presents therefore, very few materials for the comprehension of the modifications exhibited in the composition of the blood-corpuscles.

The *amount of water in the blood-cells* undoubtedly stands in a definite relation to the amount of water in the serum, as we may easily perceive from the morphological behaviour of the blood-cells on the addition of water, or dilute or concentrated saline solutions. In this point of view, the blood-cells, moreover, are constantly reacting on the intercellular fluid. Then, further, it is easy to perceive that the constituents of the blood-cells, which differ essentially from those of the plasma, must also have different degrees of diffusibility for water; and that the quantity of water contained in the blood-cells must always differ from that in the intercellular fluid. We have already seen, from Schmidt's investigations, that the solid constituents of the blood-cells are almost four times as great as those of the serum; that is to say, if 100 parts of blood-cells contain 32 solid parts, we shall find in 100 parts of serum little more than 8 parts of solid matter. In the meanwhile, the most accurate of Schmidt's investigations regarding human blood, and of my own, on the blood of the horse, by no means present a constant relation between the quantity of water contained in the blood-cells and that in the serum; but such a result was not to be expected from the differences which the cells present in their chemical constitution. This much only is certain, that when the quantity of the water is decreased in the serum, it is likewise similarly decreased in the blood-cells; and in the same manner, when an augmentation occurs in the former, it is also perceived in the latter. From the observations hitherto instituted in reference to morbid blood, it has been believed that we might establish the following general proposition:—that the quantity of water contained in the blood bears an inverse relation to the number of the blood-corpuscles; but the above remarks must have sufficiently shown that this cannot be received without a certain limitation, more especially as the rule presents numerous exceptions. The decrease in solid constituents is not limited in these cases to the solid substances of the blood-cells, but extends in a corresponding proportion to those of the serum. It is evident that where there is an absolute diminution of the blood-cells and an increase of the serum, the blood must, on the whole, be richer in water when the heavier morphological elements are diminished. When we treat of the serum, we will enter more fully into the relations on which the greater or lesser quantity of water in the blood depends.

The composition of the blood-corpuscles differs, moreover, in respect to their proximate solid constituents. We have seen that *globulin* and *hæmatin* do not stand in a definite numerical relation to each other in the coloured blood-cells. The hæmatin of different animals appears, from Mulder's researches, to be perfectly identical; and we might, therefore, draw a conclusion from the iron contained in the blood-corpuscles regarding the quantity of hæmatin. From Schmidt's calculations, which have been partly based upon direct investigations, and partly on the analyses of others, it would appear that, for every 1 part of metallic iron, there occur in the blood of men 230 parts of corpuscles (according to Becquerel and Rodier, 251); in the blood of women, 229; in that of oxen, 196·5; in that of pigs, 223; and in that of hens, 307. In the first stage of typhus, where the number of blood-corpuscles is increased, Schmidt found the proportion as 1 : 220, and hence the quantity of the hæmatin was diminished. In those conditions, however, in which the number of the blood-corpuscles is diminished, the hæmatin is relatively increased; for he found that on an average the relation between the iron and the dry blood-cells was, in pneumonia, as 1 : 248; in chlorosis, as 1 : 269; and in pregnancy, as 1 : 249. In the same manner, Schmidt made the important observation already referred to, that the blood-corpuscles become poorer in globulin and richer in hæmatin after repeated venesections, when the blood has become more watery.

Schmidt has drawn up the following table from cases in which three venesections were performed. The first was a case of pneumonia, in which the blood was analysed by himself; the second was one of tuberculosis; and the nature of the third is not specified. The analysis in the last two cases was made by Becquerel and Rodier.

	Pneumonia.	Tuberculosis.	Unspecified case.
1st venesection	248 : 1	256 : 1	252 : 1
2nd „	233 : 1	252 : 1	247 : 1
3rd „	221 : 1	234 : 1	212 : 1

The relative quantity of iron contained in the blood-corpuscles increases, therefore, with each successive venesection. This phenomenon admits of a simple solution, for it would appear, from all observations, that the hæmatin cannot permeate the walls of the blood-cells, which, however, admit of the permeation of their albuminous contents: now if the blood loses solid constituents, the serum becomes richer in water; a diffusion-current of a more diluted solution then enters the blood-cells, whilst a more concentrated stream passes outwards from them; now since hæmatin cannot penetrate through the cell-wall, the loss of solid constituents from the blood-cell must mainly affect the globulin, whilst the hæmatin will, under such conditions, appear to be relatively increased in relation to the globulin + the cell-membrane.

I found the quantity of hæmatin in the cells of the arterial blood of the horse somewhat more considerable than that contained in the blood of the external jugular veins; whilst, on the other hand, the quantity of hæmatin contained in the blood-cells of the hepatic veins is far smaller than that of the portal blood.

I found the ratio of iron to the dried blood-corpuscles in the arterial blood of the horse, as 1 : 394; in the jugular vein, as 1 : 390; in the portal vein, as 1 : 312; and in the hepatic veins, as 1 : 500; these being the mean results obtained from several experiments. The smaller quantity of hæmatin contained in the cells of the arterial blood, compared with those of the jugular venous blood may be referred not only to the greater richness in fat of the arterial blood, but more decidedly, or even exclusively, to the loss of fat which takes place during the arterialization of venous blood by the process of respiration.

In speaking of the formation of blood-cells in the liver, we drew attention to the fact that a small portion of the iron which was conveyed to that organ with the blood-cells of the portal vein, is separated with the bile, while the remaining portion appears to be equably distributed among the blood-corpuscles which have been newly formed within the liver, so that the iron of 100 blood-corpuscles of the portal vein is distributed over nearly 150 corpuscles of the hepatic veins: consequently the blood-cells of the hepatic veins must contain one-third less iron than that of the portal vein.

The blood-corpuscles must necessarily also exhibit differences in their amount of *fat,* since the quantity of fat contained in the blood of different animals and of men, under different conditions, is extremely variable. In reference to this question, I have directed special attention to the differences in the quantity of fat contained in the blood-corpuscles of different vessels of the same animal; and the results of my investigations, taking the mean of several experiments, are, that 100 parts of *moist* blood-cells from the carotid artery of a horse contain 0·608 of fat; 100 parts from the external jugular vein, 0·652; from the portal vein, 0·752; and from the hepatic veins, 0·684. These experiments warrant us in hoping that a further prosecution of such inquiries may throw a very considerable amount of light on the metamorphosis of fat, and on the function of the blood-cells. The first step seems, at all events, to have been made towards the elucidation of that chemical metamorphosis which the blood-cells experience in the pulmonary capillaries by the action of the inspired oxygen.

That the blood-corpuscles contain variable quantities of *soluble salts,* is a fact that is made evident by the above mentioned investigations of C. Schmidt, in which he ascertained the different proportions of the potash salts and phosphates in the blood-cells to the soda and chlorine compounds in the serum of the blood of different species of animals. But I also found that the quantity of salts contained in the cells of the blood from different vessels of the same animal constantly differed; thus, for instance, 100 grammes of fresh blood-cells from the temporal artery of a horse contained 0·806 of a gramme of salts (independently of the peroxide of iron in the ash); the same quantity, taken from the external jugular vein, contained 0·632, from the portal vein 0·729, and from the hepatic veins 0·893. There is therefore a very considerable difference, in reference to their amount of salts, between the cells of the arterial and those of the venous blood; the former containing more salts than those of ordinary venous blood. The relation between the cells of the portal vein and those of the hepatic veins is still more striking; for although the serum of the portal blood is far richer in salts than that of hepatic venous blood, the difference in the amount of salts in the cells of the two kinds of blood is still more strongly marked.

This excess of saline contents in the arterial blood-cells can only be explained by the loss of other substances, as, for instance, fat and perhaps also extractive substances, which are lost by the venous cells in their passage through the capillaries of the lungs; this increase of the salts during the arterialization of the blood-cells is, therefore, probably only a relative one. The case is wholly different with respect to the saline contents of the cells of the blood flowing to and from the liver. If, as would seem probable from our investigations on the subject, new corpuscles are actually formed in the liver, it follows from this fact that the younger blood-corpuscles contain more salts and less hæmatin than the older cells of the blood of other vessels, and that a certain quantity of salts passes from the serum of the portal vein into the blood-cells of the hepatic veins. This increase of salts in the cells of the blood of the hepatic veins is principally limited to phosphates and chlorides, as I constantly found in three comparative investigations. In 100 parts of fresh blood-cells of the portal blood I found, on an average, 0·1593 of chlorine and 0·0578 of phosphoric acid in combination with alkalies; while 100 parts of cells from the hepatic veins contained 0·1796 of the former and 0·0611 of the latter.

Schmidt's investigations on the constitution of the blood during *excessive transudative processes* have thrown considerable light on this subject, and shown the differences manifested in the quantity of salts contained in the blood-cells. In cholera, where the blood loses large quantities of salts in addition to water, the blood-corpuscles are also implicated. The intercellular fluid especially loses large quantities of water and chloride of sodium; and this fluid, reacting on the blood-cells, abstracts not only a portion of their water, but also a portion of their salts. As the potash compounds and the phosphates predominate in the blood-cells, it is these salts which chiefly escape into the plasma; consequently these compounds are more abundant in the serum in cholera than in a state of health. Hence in cholera, the blood-corpuscles become relatively richer in solid organic matters, while they lose a portion of their soluble salts. Schmidt found that in the blood-cells of healthy blood the ratio of water to the solid constituents was as 2·14 : 1; in the blood of cholera patients as 1·77 : 1; that the ratio of the organic to the inorganic constituents in the cells of healthy blood was as 40 : 1, and in the blood in cholera as 58 : 1. Schmidt, moreover, found an analogous and only gradually differing relation in the blood after the administration of drastic purgatives, since here the mechanical metamorphosis corresponded entirely to that set up by the cholera process. In other transudative processes, where the loss experienced by the blood principally affects the albuminates and consequently the organic matters, (as in dysentery, Bright's disease, and dropsy from different causes,) Schmidt found precisely opposite relations; for the blood-cells present this analogy with the plasma, that while the organic matters decrease in quantity, the relation of the mineral substances to the water remains nearly the same. The ratio of the water to the solid constituents in the blood-cells may be as high as 2·4 : 1, while that of the organic to the inorganic substances may be as high as 28 : 1. The salts, however, according to Schmidt's investigations, remain in the same relative proportions to one another in the cells of blood of this kind as in those of healthy blood.

Very little is known positively regarding what are called the *extractive matters* of the blood-cells; in 100 parts of fresh cells of horses' portal blood, I found on an average 0·482, and in those of hepatic venous blood 0·988 of extractive matters free from salts. We shall find that these substances occur in a far larger quantity in the intercellular fluid of the hepatic venous blood than in that of the portal blood.

In healthy blood the colourless are to the coloured corpuscles in the ratio of 1 : 8 (according to R. Wagner). As the red corpuscles are rendered invisible by the addition of water to the blood, we may in this manner form an approximate estimate of their quantity; in the inflammatory crust, however, this may be best done by acetic acid, which renders the fibrinous coagulum perfectly transparent under the microscope, and makes the cells embedded within it much more distinctly apparent. Their quantity in the blood is considerably increased during digestion; after fasting, they almost entirely disappear; at all events this may be observed in frogs kept without food. A diminution in their number is less rarely observed than an augmentation. Remak noticed their extraordinary increase after copious venesection. According to Nasse and Popp, their number is often considerably increased in pneumonia and tuberculosis, but this is not constant; in typhus and chlorosis they do not appear to be sensibly altered in quantity. In pyæmia, these cells are certainly often very considerably increased in the blood, but this augmentation has been rather inferred from the so-called metastatic abscesses, than directly observed. The blood is, however, sometimes found to contain a great number of colourless corpuscles in conditions in which there cannot be any purulent resorption, as, for instance, in the case of dogs affected with cutaneous eruptions.

We will now proceed to the consideration of those modifications in the chemical *composition of the intercellular fluid,* which have been observed to occur under different physiological and pathological relations, and will endeavour to arrange them according to the augmentation or diminution of the individual constituents. We will begin with the *fibrin;* but as we have already considered the most important points in reference to this subject (see vol. i., p. 357), little more remains to be noticed regarding it.

Opinions are not wholly agreed as to the quantitative difference of the fibrin in *venous* and in *arterial blood,* although Lecanu and Nasse coincide in believing that arterial is richer in fibrin than venous blood; and in this respect their opinion corresponds with my own experiments on horses' blood, in which I found 6·814 p.m. of fibrin in the arterial blood, and 5·384 p.m. in the jugular venous blood; but while the quantity of fat in the blood-cells and in the serum differed in both kinds of blood, it was almost perfectly equal in the arterial and in the venous fibrin (namely, 2·154% in venous and 2·168% in arterial dry fibrin). I found rather more ash (2·172%) in the fibrin of arterial than in that of venous blood (1·907%). The fibrin of arterial blood coagulates more rapidly than that of venous blood. In both kinds of blood, when taken from the horse, there is generally formed a superficial layer of fibrin; but this is much more extensive in venous blood, and also more distinctly limited by the clot, than in arterial blood, which may perhaps be mainly owing to the more rapid coagulation of the arterial fibrin, rather than to the less rapid sinking of the cells of the arterial blood, for these are specifically heavier than the venous blood-corpuscles (being poorer in fat and richer in hæmatin), and should therefore sink more rapidly.

In reference to the difference in the quantity of the fibrin contained in *portal* and in *hepatic venous blood,* I may simply remark that, as has been already stated, I found from 4 to 6% of fibrin in the portal blood, whilst in hepatic venous blood there were only traces of fibrin, and sometimes no *true* fibrin whatever. In the fibrin of the portal blood I found from 6·1 to 7·8%, and F. C. Schmid from 7·4 to 8·7% of fat.

Schmid describes the fibrin of the portal blood as a greasy, viscid, or gelatinous mass. In horses which had been fed some (5 to 10) hours before death, I found the fibrin precisely similar in character to that of jugular venous blood; it likewise always formed a very dense and consistent crust in coagulated portal venous blood. Moreover, I could not discover that this fibrin was very readily soluble in a solution of nitre.

We will now proceed to consider the *constituents of the serum*, and in the first place the *quantity of water* which it contains in different conditions. On this subject we are also indebted to Nasse for our most accurate information. We need not here again repeat that the quantity of water in the serum influences the quantity in the blood-cells, and that consequently the following statements, regarding the augmentation or diminution of the water, may be regarded as referring to the whole mass of the blood. All experimenters, without exception, concur in the statement that the serum of *women* is richer in water than that of *men;* and the most recent comparison of the two kinds of blood (that, namely, by Schmidt) yields the same result; in the serum of man's blood Schmidt found 90·884%, and in that of woman's blood 91·715% of water. In *pregnancy* the blood is still richer in water. Serum obtained from the *placenta* contains, according to Poggiale,* less water than that from *new-born infants;* the blood of new-born infants, however, contains less than that of adults; in old age the quantity of water again visibly rises. Nasse, on the other hand, found that the blood of the embryonic animal was richer in water than that of the mother.

In different *animals* the quantity of water in the serum and in the blood presents considerable variations; Prevost and Dumas, Berthold, Nasse, and more recently Poggiale, have instituted extensive series of comparative investigations; notwithstanding many differences in individual details, the results of these observers coincide in the following points: namely, that the serum of the amphibia contains the largest amount of water, and that of birds, on an average, a larger quantity than that of the mammalia; and that of the latter class, the serum of swine contains the least, and that of goats and sheep the most water.

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* Compt. rend. T. 25, p. 198-201.

In regard to the quantity of water in the serum of blood from *different vessels,* the following may at all events be laid down as a general rule: the serum of arterial blood is more watery, and hence specifically lighter, than that of venous blood, according to the experience of most observers (although Lecanu and Letellier maintain the contrary); in the serum of the blood of the temporal artery of a horse I recently found 89·333%, and in that of the external jugular vein 86·822% of water. Zimmermann* found the serum of the veins of the lower or hinder extremities (of men and animals) poorer in water than the upper or anterior ones.

The *serum of the portal vein* is richer in water than that of any other vein, according to the unanimous opinions of Schultz, Simon, and F. C. Schmid, who have all experimented on the subject. My own experiments lead me to believe that this depends both on whether or not the process of digestion was going on at the time, and on whether or not the animals had taken much fluid shortly before their death. Under these different relations I found from 92·342% to 88·684% of water in the serum of portal blood. The serum of hepatic venous blood is always far richer in solid constituents than that of portal blood; in five cases I found the quantity of water in the latter to vary between 89·420% and 89·298%, a result whose importance in relation to the function of the liver has already been noticed (see p. 103).

This leads us to revert to the relation which the amount of water in the serum and in the blood generally bears to the number of blood-corpuscles. It is a striking phenomenon, that *ordinarily* a blood whose serum contains much water, presents few corpuscles; we observe this in blood under various physiological relations (and even in the blood taken from different vessels), but especially in morbid blood; hence, the richer a specimen of blood is in water, so much the more serum or intercellular fluid does it contain: if, however, this is a general rule, it is by no means a law, for we not only meet with exceptions to it, but the most accurate analyses made with special reference to this point fail to establish any constant ratio. Thus, for instance, in hepatic venous blood there may be from 137 to 351 parts of fresh blood-cells associated with 100 parts of serum containing from 89·3 to 89·4% of water. In morbid blood we still more often meet with similar cases. Hence neither of these properties of the blood depends upon the other, but they are co-ordinate phenomena;

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* Arch. f. phys. Heilk. Bd. 6, S. 587-600.

that is to say, the conditions which give rise to a diminution of the solid constituents of the serum, generally, at the same time, also occasion a diminution of the coloured blood-cells.

It is very difficult to ascertain whether copious draughts of fluid occasion a temporary augmentation of the water in the serum, in consequence of the rapidity with which an excess of water is removed from the blood. Schultz* thought that he had convinced himself by direct experiments on oxen, that the blood presented a relative augmentation of water after the copious use of that fluid; Denis, on the other hand, denies that this is the case, at all events in man. But that the solid constituents of the serum should suffer diminution in the absence of proper nourishment, and that there should thence be an augmentation of water, is only what might be expected; and is confirmed by all the investigations that have been made either with healthy or diseased blood, when the persons from whom it was taken had been deprived for a long time of all nutriment, or had been only poorly and scantily fed.

Since in the great majority of *diseases* comparatively little food is taken in consequence of the loss of appetite or the prescription of low diet, and the resorption of nutriment only proceeds imperfectly, or finally essentially nutritious matters are lost by profuse excretions or by copious losses of the juices, (as for instance, repeated blood-lettings), it follows, that in consequence of the imperfect restitution of the substances which have been normally or abnormally lost, the blood must become poor in solid constituents. Hence the analyses of the blood in most diseases show that it is specifically lighter, that is to say, poorer in solid constituents, than normal blood. This poorness of the blood in solid constituents is not, as a general rule, associated with a diminution of the collective mass or volume of the blood circulating in the vessels; for in our consideration of the mechanical metamorphosis of matter, we shall be led to the result, that the blood has a constant tendency to retain its original volume, so long as the whole mechanism is not disturbed. Hence if solid substances are abstracted from the blood in disease, and are not again replaced, this fluid not only appears watery, in consequence of its containing less solid constituents, but also from its having taken up more water than it contains in the normal state. In such cases the quantity of water is not only relatively, but absolutely increased in the blood. Even in the beginning of most diseases, especially those of an acute character, we find the blood more watery than

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* Hufeland's Journ. 1838. H. 4, S. 291.

usual, except during the first ten days of typhus, during cholera, and scarlatina and measles in their first stages; although not unfrequently we find the serum denser and richer in solid constituents than the normal fluid, or at all events, as dense and rich. Hence, it must be concluded that, immediately after the primary invasion of certain diseases, the blood-corpuscles are destroyed in large numbers, or at all events are not renewed in sufficient quantities, and that their products of metamorphosis are retained for some time in the serum, and thus increase its solid constituents, or at all events balance its loss. In the further course of acute diseases (with the exception of cholera), the solid constituents of the serum are always diminished, and its specific gravity falls more or less below the normal standard. The only exceptions to this rule occur in the case of acute articular rheumatism, erysipelas, and puerperal peritonitis; in these diseases there is an extraordinary diminution of the blood-corpuscles, so that the whole blood assumes an abnormally watery appearance, while the serum is denser and contains more solid constituents than in the normal state.

There are certain chronic conditions to which we have applied the names of *anæmia* and *hydræmia*, and which are consequences of severe acute diseases, and especially of such as are associated with considerable losses of the juices, colliquative discharges, or thoroughly destroyed nutrition. The ideas which we are in the habit of connecting with these names are often not sufficiently distinctive. We are accustomed to associate the form of disease which we name chlorosis with both these states, and especially with anæmia. But if, by the term anæmia, we understand an absolute diminution of the blood and of its solid constituents, chlorosis does not fall within the conditions of anæmia; and independently of pathological grounds, the chemical composition of the blood is opposed to this view, for in chlorosis, neither the whole volume of the blood nor the amount of solid constituents in the serum is diminished, but only the number of the blood-corpuscles. Becquerel and Rodier* have recently examined the serum with much care in various diseases, and have found that the serum of chlorotic patients presents a perfectly normal constitution. If plethora actually depended on an absolute increase of the blood circulating in the vessels, the not very unfrequent occurrence of plethora in chlorosis would also stand opposed to our attaching identical ideas to the terms chlorosis and anæmia. There is no scientifically accurate proof that there is an actual diminution of the whole mass of the blood,

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* Gaz. de Paris. No. 33 et 36, 1846.

and no such conclusion can be drawn from the appearances after death; hence, if a true diminution of the blood does not exist, our idea of anæmia would entirely coincide with that of hydræmia; and in point of fact, it is in most cases mistaken at the bed-side, and confounded with hydræmia. The causes of hydræmia, that is to say, of a great excess of water in the blood, and especially in the serum, are sufficiently obvious from the preceding observations. Hydræmia, like dropsy, is only the consequence of an abnormal state of certain organs, for the one necessarily follows the other, each being dependent on purely physical laws; if the blood becomes more watery, the albumen more readily transudes through the capillaries of this or that organ, especially where the motion of the blood is somewhat impeded, and hence the frequency of œdema of the feet; if albumen passes away with the urine, the blood becomes poorer in solid constituents, and the serum more readily transudes; hence, dropsy is a constant attendant on Bright's disease. If, however, dropsy appear sooner than hydræmia, the latter must be the necessary consequence of the former, if abundant transudations of albumen render the blood more watery, without this condition being counteracted by a sufficient renewal of nutriment from without. (C. Schmidt.*)

A decided and absolute *diminution of the water* in the serum, and in the blood generally, is in reality only observed in cholera; on this point all observers concur: the watery character of the dejections in cholera, which often contain only from 0·3 to 0·5% of solid constituents, afford a ready explanation of this peculiarity.

In addition to the diseases already mentioned, viz., acute articular rheumatism, puerperal peritonitis and erysipelas, there is also a diminution of the water in the serum, although only a relative one, in chronic diseases of the heart. If, however, symptoms of dropsy have already supervened, we always find that the serum contains an abnormal excess of water.

Before leaving this subject we must remark, that in addition to the proposition that the water of the blood always stands in an inverse relation to the blood-corpuscles, we have also established the aphorism, that the quantity of water in the blood is always proportional to its quantity of fibrin. We must, however, remark that this statement must not be taken literally, that is to say, in a mathematical sense, for we are unable to deduce any formula expressing such a relation. On instituting a comparison between the most accurate analyses which we possess, we just as often find

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* Characteristik der Cholera. S. 116—151.

a great augmentation of the fibrin as a diminution of the solid constituents of the blood and of the serum, and the latter are often far more diminished, than the fibrin is increased. Hence it is impossible to refer the augmentation of the fibrin in inflammation, in a direct manner, to the diminution of the albumen, that is to say, to explain the augmentation of the fibrin by a too early metamorphosis of the albumen into this substance, as some have attempted to do. All that we are justified in asserting is this: in those physiological and pathological conditions which are accompanied by a greater or smaller augmentation of the fibrin, we are in the habit of simultaneously observing a diminution of the coloured blood-corpuscles, and a greater or less augmentation of the water of the blood, but by no means always of that of the serum; for, to take an example, in acute articular rheumatism, a disease in which the fibrin is often very much increased, we find, on the contrary, the quantity of water in the blood diminished, relatively to the quantity of the solid constituents of the serum; in hydræmia the quantity of water in the serum is extraordinarily increased, while the fibrin scarcely exceeds the normal limits.

We now proceed to the consideration of the *albumen*, of whose occurrence and relations in the blood we have already treated generally (see vol. i., p. 342).

The amount of albumen in the serum generally rises and falls with that of the other solid constituents; unfortunately, however, most investigations of the blood are limited to the mere determination of the solid residue of the serum, so that we have often no means of determining the ratio in which the latter and the albumen stand to each other: indeed no true conclusion can be drawn from most analyses of morbid blood (previously to those of Scherer and C. Schmidt), not merely because the mode of determining the albumen was unsuitable, but also because we paid too little attention to, or were unable accurately to investigate, the relation of the intercellular fluid to the blood-cells. In order to draw a scientific conclusion from such investigations, it is by no means sufficient to recognise an absolute or a relative augmentation or diminution; it is a much more important point to determine specially in relation to which constituents of the blood the albumen has been increased or diminished; it is not till these highly important relations are followed out in detail, that we can arrive at any inductive conclusions regarding the nature of the pathological changes. Such a general study of the quantitative relations of the albumen in diseased blood, is the means by which we may hope to attain to a true humoral pathology; for, doubtless, all the metamorphoses in the blood proceed from the albumen. We must bear in mind the numerous conditions by which the quantity of albumen in the blood may be changed; this may be effected, not merely by augmentation or diminution of the serum or of the water, but also of salts or extractive matters, by absorption of albumen from the other juices or its loss by exudations or copious excretions, by rich and abundant nutriment, &c. A glance at merely those analyses in which the albumen of the blood has been actually determined by a good method, will indicate the difficulties of attempting to answer such questions.

The quantity of albumen in venous blood increases considerably during digestion.

F. C. Schmid found on an average 6·68$\frac{0}{0}$ of albumen in the serum from the jugular veins of horses which had been starved for a long time before they were killed; while in corresponding serum, when the animals had been fed shortly before their death, he found 9·08$\frac{0}{0}$.

There is less albumen contained in *arterial* than in *venous* blood, as was discovered long ago by F. Simon. In the serum of the venous blood of the horse I found 11·428$\frac{0}{0}$, and in that of the arterial blood 9·217$\frac{0}{0}$ of albumen. In the residue of the serum of the venous blood there were, however, 15·3 parts of extractive matters and salts to 100 of albumen; while in that of the arterial blood there were 15·7 parts of extractive matters to 100 of albumen.

The serum of *portal blood* is regarded as poorer in albumen than that of the jugular veins; Schmid found on an average 5·19$\frac{0}{0}$ of albumen in this serum when obtained from fasting horses, and 6·71$\frac{0}{0}$ when they had been well fed; in horses which had been fed from 5 to 10 hours previously to their being killed, I found from 6·015 to 6·997$\frac{0}{0}$ of albumen. In the solid residue of the portal serum I found that the albumen stood to the other constituents in the ratio of 100 to 22·5, the horse having been killed five hours after feeding.

The albumen in the *serum of the hepatic venous blood* of horses which were killed from 5 to 10 hours after feeding only varied between 10·487 and 10·702$\frac{0}{0}$; hence the serum of the blood of the hepatic veins is far richer in albumen than that of the portal or jugular veins; but if we compare the other solid constituents of the serum with the albumen, we find a diminution of the albumen in the serum of the hepatic veins, as contrasted with that of the portal vein; for while I found the ratio of the albumen to the other solid constituents to be 100 to 22·5 in the serum of the portal blood, it was as 100 to 38·4 in that of the hepatic venous blood. That the albumen in the blood of the hepatic veins is not merely relatively, but also absolutely diminished, is moreover obvious from the composition of the collective blood; in the portal blood we find far more serum than in the blood of the hepatic veins; so that on an average I found that the albumen of the portal blood was to that of hepatic venous blood in the ratio of 3 : 2.

When the intercellular fluid of 1000 parts of portal blood contained 24·453 parts of albumen, 16·553 parts were found in the intercellular fluid of an equal portion of hepatic venous blood; hence the albumen in the two intercellular fluids was in the ratio of 100 : 67·7; in another case the ratio was as 29·606 : 19·806, or as 100 : 66·9; and in a third case (10 hours after feeding) as 44·330 : 32·447, or as 100 : 73·1. Hence, from these numbers, we cannot entertain a doubt that on an average 30·2$\frac{0}{0}$ of the albumen conveyed to the liver is converted in this organ into other substances, and is probably for the most part applied to the formation of cells.

The reason why Simon* found so few blood-corpuscles in the blood of the hepatic veins, is entirely dependent on the analytical method which he employed.

The amount of albumen has been found to be diminished in the following *diseases:* in simple ephemeral and remittent fevers (only slightly diminished), in severe inflammations, in the later stage of typhus (Becquerel and Rodier), in scurvy (where, as is shown by Andral and Gavarret, Becquerel and Rodier, and Favre,† it is considerably diminished), in malaria (Salvagnoli and Gozzi‡), in puerperal fever (Scherer§), in dysentery (Leonard and Folley,‖ and C. Schmidt), in Bright's disease, and in dropsy from various organic changes (as was asserted by the older observers, and accurately demonstrated by C. Schmidt). The quantity of albumen in the serum has been found to be increased in intermittent fevers (Becquerel and Rodier), after drastic purgatives, and in cholera (C. Schmidt).

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* Journ. f. prakt. Ch. Bd. 22, S. 118.

† Compt. rend. T. 25, p. 1136.

‡ Gaz. de Milano. No. 30, 1843.

§ Untersuchungen, &c. S. 74—69.

‖ Rec. des Mém. de Chim. et de Pharm. milit. T. 60, 1846.

Little importance has generally been attached to the *quantity of fat* in the serum, and we possess very little positive knowledge regarding the quantitative relations of this substance in different physiological and pathological conditions. In most cases in which a determination of the fat has been attempted, this determination has had reference to the blood collectively, so that we have comparatively little information regarding its distribution between the blood-cells and the serum.

It appears from the experiments of Simon, Nasse, Becquerel, and others, that in normal blood-serum the fat ranges from 0·2 to 2·22% of the solid residue.

For further information regarding the quantity of fat contained in the blood generally, we must refer to vol. i., p. 249.

Although it would appear from the experiments of Boussingault, to which we have already referred, that the use of fat (taken as food) does not induce any augmentation of the fat in the blood, yet nutrition is not without influence on this constituent of the circulating fluid; for during the progress of the digestive process, not only have the chyle and the portal blood been found richer in fat, but sometimes also the serum of the blood generally has been actually observed to be rendered turbid by the presence of this substance (Thomson*). Schmid, moreover, found that the serum of horses that had been recently fed contained almost twice as much fat as that of horses which had been kept fasting.

A horse on which I was experimenting was fed for three days entirely on starch-balls. Immediately before and after this course of diet I abstracted and analysed the blood from the carotid artery and the jugular vein. The result of this investigation, in reference to the amount of fat, will probably be best shown by the following tabular arrangement.

The quantity of fat

		Before this food.	After this food.
Clot	From the carotid artery	1·996	1·665
	From the jugular vein.	2·924	1·366
Serum	From the carotid artery	2·479	1·465
	From the jugular vein	2·984	2·226

This experiment throws light not merely on the constant difference between arterial and venous blood, but also on the influence of an imperfect nutrition—as that of an exclusive starch-diet—on the diminution of the fat in the blood. The number

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* Phil. Mag. 3rd Series, Vol. 26, pp. 322 and 418.

representing the amount of fat contained in the venous clot after the use of the starch, may perhaps be influenced by an error of observation.

The blood of women is, according to Becquerel, generally somewhat richer in fat than that of men.

The serum of *arterial* blood contains less fat than that of *venous* blood: in this respect my results coincide with those of Simon; in the arterial serum of a horse I found 0·264% of fat, which amounted to 2·479% of the solid residue; while in the venous serum I found 0·393%, or 2·984% of the solid residue. In the *serum from the jugular veins* of starved horses, Schmid found that the fat averaged only 0·07% (or 0·93% of the solid residue), while in horses that had been well fed it amounted to 0·13% (or 1·14% of the solid residue).

The difference between the results of my experiments and those of Schmid may appear striking; I must, however, remark that the blood of the horse whose arterial and venous blood were examined before and after the three days' exclusive feeding on starch, contained more fat than that of any other horse I ever met with; this also throws some light upon the numbers (quoted in the next paragraph) which I obtained in a comparative determination of the fat in the portal and the hepatic venous blood, and which are singularly small, although these kinds of blood usually contain more fat than ordinary arterial or nervous blood. The blood-cells of this horse did not contain any corresponding augmentation of fat (as may be seen from the previously quoted numbers), so that the great abundance of fat which was presented both by the venous and arterial blood of this horse was entirely limited to the serum. I do not find it recorded in my note-book that the serum was turbid, or that fat-globules were perceived under the microscope.

The serum of *portal blood* is, according to Schultz and Simon, far richer in fat than that of jugular venous blood: in the portal serum of fasting horses, Schmid found on an average 0·10% of fat (or 1·36% of the solid residue), and in that of well-fed horses 0·21% (or 2·06% of the solid residue); I found on an average 0·2843% of fat (or 3·645% of the solid residue) in the portal serum of horses which had been fed from 5 to 10 hours previously.

The serum of the *blood of the hepatic veins* contains far less fat than that of the portal blood, but far more than that of the jugular veins; on an average I found it to contain 0·2722% of fat, or 2·568% of the solid residue.

It is scarcely necessary to remark, that on instituting a comparison of the whole blood (serum + blood-cells + fibrin), the difference which these two kinds of blood present in their amount of fat is far more obvious, because portal blood contains a preponderating quantity of serum, and the hepatic venous blood a comparatively small quantity. The numbers representing the relative amounts of fat are given in p. 88.

The most careful investigations regarding the quantity of fat contained in the serum in different diseases have been instituted by Becquerel and Rodier; from their researches it follows, that almost from the beginning of every acute disease there is an augmentation of the fats in the blood, and especially of the cholesterin. In chronic diseases the fats and principally the cholesterin are especially increased in hepatic affections, as, for instance, icterus and cirrhosis, as well as in Bright's disease, tuberculosis, and cholera.

In the *blood of animals* the quantity of fat appears to be very variable under apparently similar relations; at all events, one and the same observer (as, for instance, Nasse) has found very different quantities of fat in the blood of the same species of animals. This subject has been already noticed in vol. i., p. 249.

Nasse[*] found the smallest quantity of fat in the blood of goats and sheep, rather more in that of horses, and still more in that of dogs: the blood of the pig, however, contained no more than that of the dog. While the blood of puppies contained more fat than that of adult dogs, the blood of calves, on the other hand, contained less fat than that of oxen.

Few chemists have extended their inquiries to the determination of the quantity of the *extractive matters* contained in the serum; at all events, they are always determined in association with the salts; the number representing them might certainly be calculated from many analyses, if we did not fear, on the one hand, by including the loss incurred in the entire process, to obtain too high a number, or on the other hand, by imperfect drying, to get by far too low a number. But even when the quantity of the extractive matters has been directly determined, I find from my own investigations, and those of others, that their number is liable to great fluctuations, ranging from 0·25 to 0·42%. When we consider how many things are vaguely included in extractive matters, and how these latter are augmented by the products both of pro-

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[*] Journ. f. prakt. Ch. Bd. 18, S. 146.

gressive and regressive metamorphosis, we need no longer wonder at these fluctuations.

Nasse has found more *extractive matters* in the blood of *children* and *young animals* than in that of the adult species; the largest quantity was found in human blood, rather less in that of horses, and a much smaller amount in that of oxen.

From the few analyses which I have made with horses' blood, I have been led to the conclusion that more extractive matter is contained in *arterial* than in *venous* blood; while the solid constituents of venous serum contained on an average 3·617% of extractive matters, those of the arterial serum contained 5·374%.

The serum of *portal blood* contains more extractive matters (always determined as free from salts, by the incineration of the ethereal extract freed from fat by water, and of the alcoholic and aqueous extracts) than that of the jugular venous blood; the serum of the *blood of the hepatic veins* contains, however, the largest quantity of extractive matters. In horses which had been fed (from 5 to 10 hours) previously, I found on an average 7·442% of extractive matters (free from salts) in the solid residue of the serum of the portal blood, and a larger quantity, namely, 10% when the animals had fasted for 24 hours: but from the blood of the hepatic veins I constantly found more than 18% (from 18·1 to 18·5%).

Amongst the *diseases* in which the extractive matters are increased, we may especially notice puerperal fever (Scherer) and scurvy.

For the quantitative determination of the *salts* contained in the serum, it is above all things necessary that we should accurately know the ratio in which the number representing the mineral substances obtained by incineration stands to the number representing the salts which exist pre-formed in the blood, and the manner in which the acids and bases of the ash are grouped in the fresh serum; we know, however, from what has been previously stated, that we too often find great differences in the constitution of the ash, which depend upon the methods we may have adopted for the carbonisation and incineration of animal substances. Hence it follows that, notwithstanding the careful labour which so many inquirers have devoted to the determination of the saline constituents of the blood, the results in question present little uniformity, or, at all events, are of such a character as to preclude us from basing any conclusions on them.

From the best analyses it would seem that the ash of the serum is composed much in the following manner:

Chloride of sodium	61·087
Chloride of potassium	4·054
Carbonate of soda	28·880
Phosphate of soda ($2\,NaO,PO_5$)	3·195
Sulphate of potash	2·784
	100·000

The serum of men's blood, contains generally rather a larger amount of salts than that of women's blood ; the former containing on an average 8·8%, and the latter 8·1% ; but the limits between which the amount of salts in the serum of both sexes in the normal state may fluctuate, are tolerably extensive.

According to Nasse and Poggiale*, there is a larger amount of salts in the serum of adult men and animals, than in that of children and young animals.

It would appear from the investigations of Nasse and Poggiale, that there is no connexion between the saline constituents in the blood of a animal, and the nature of its food ; according to these chemists, the blood of cats, goats, sheep, and calves, contains the most salts, then follows the blood of birds, and then that of men and swine ; whilst the blood of dogs and rabbits contains the least.

Nasse found most *alkaline phosphates* in the blood-ash of swine, geese, and hens, and least in that of goats and sheep ; he found most *sulphate of soda* in that of sheep, and least in that of hens and geese ; most *alkaline carbonates* in that of sheep, and least in that of geese and hens ; and most *alkaline chlorides* in that of goats and hens, and least in that of rabbits.

Moreover, the serum of the blood of *different vessels* contains different quantities of salts ; from my own investigations and those of Nasse, it appears that arterial serum contains rather more salts than venous serum. Schultz, Simon, and Schmid, found far more salts in the blood of the portal than in that of the jugular vein. (Schmid found at least half as much again.) Moreover, the serum of portal blood contains far more salts than that of hepatic venous blood ; in horses we find on an average 0·850% (or 10% of the solid residue) in the former, and only 0·725% (or 7% of the solid residue) in the latter. If to this we add that there is far less serum in the blood of the hepatic veins than in that of the portal vein, it is obvious that the blood of the latter is far richer in salts than that of the former.

By the prolonged use of food rich in common salt, the blood

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* Compt. rend. T. 25, pp. 109—113.

becomes richer in saline constituents, and especially in chloride of sodium. (Poggiale and Plouviez.*)

Zimmermann† has found in five experiments made on men, and one observation on a horse, that there is always a larger quantity of soluble salts in the last portion of the blood of one and the same venesection, than in the first portion; and that this augmentation is chiefly due to the alkaline chlorides, the other salts being diminished.

In *diseases* the alkaline salts of the blood undergo considerable fluctuations; but on this point most of the blood-analyses hitherto made are very imperfect; this much only is certain, that in severe inflammations these salts are very much diminished, and that in the acute exanthemata and in typhus they are very much increased. Moreover, C. Schmidt has especially noticed that there is a considerable diminution of the soluble salts in the serum of cholera blood, and an augmentation in dysentery, Bright's disease, and all kinds of dropsy and hydræmia. Finally, it has been found by Leonard and Folley, as well as by Salvagnoli and Gozzi, that the salts are often increased to twice their normal quantity in several endemic diseases, namely, dysentery, malaria, the malignant forms of intermittent fever, scurvy, &c.

It would be highly important to know the amount of *gases* contained in the blood in different physiological and pathological conditions; indeed we hold that it is from this point that a rational investigation of the blood should commence, if we wish to take a philosophical view of its general constitution. All conclusions which we think we can draw from blood-analyses, remain mere conjectures so long as each individual case is not tested by an accurate determination of the gases contained in the blood. Any one desirous of instituting a good analysis of the blood, will not fail to find the means of determining quantitatively the gases of the blood in different diseases; if such an analysis be difficult, it is, at all events, not impracticable, unless physicians adhere to what is now regarded the "rational treatment," and abstain altogether from prescribing venesection. At present we have no certain knowledge on the subject, beyond the results quoted in page 191, for which we are chiefly indebted to Magnus.

We have still to notice some of the more uncommon constituents of the blood, or such as occur in mere traces. We have already mentioned that *sugar* is an integral constituent of the serum. In

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* Compt. rend. T. 25, pp. pp. 109—113.

† Heller's Arch. Bd. 3, S. 522—530.

the blood of oxen, C. Schmidt found from 0·0069 p.m. to 0·0074 p.m. of fermentable sugar; in the blood of a dog 0·015 p.m.; and in that of a cat 0·021 p.m. In the serum of portal blood, in the few cases in which I obtained enough to enable me to detect sugar, I found from 0·0038, to 0·0052 p.m., and in the blood of the hepatic veins, from 0·041 to 0·059 p.m.; in the blood of diabetic patients, where its existence had often been demonstrated, I never could find more than 0·047 p.m. of sugar.

We have already noticed (in vol. i., page 217) the quantities in which, according to Garrod, *uric acid* occurs in normal and morbid blood.

The amount of *urea* in the blood has not yet been quantitatively determined; if, however, as has been maintained, urea can be detected in four ounces of healthy blood (see vol. i., page 165) its quantity could certainly be easily determined in morbid blood; but this is *not* the case.

Silica was first discovered by Henneberg in the blood of hens, and was determined quantitatively by Millon (see vol. i., p. 427).

We have already (in vol. i., page 453), alluded to the occurrence of *carbonate of ammonia* in morbid blood; its quantitative determination is impracticable. We would merely add that it has recently been also found in the blood of cholera patients both by C. Schmidt and by myself. While I could detect urea in the blood of such cholera patients as succumbed before the occurrence of the group of symptoms to which we apply the term uræmia, I always found the blood ammoniacal, and the gastric mucous membrane in the dead body strongly alkaline as soon as the cerebral symptoms peculiar to uræmia had once set in. Moreover, from the analogous experiments which I have instituted with the blood in Bright's disease and scarlatina, I might have been led to the conclusion, that it is not the presence of urea, but of ammonia, in the blood, which occasions the symptoms of uræmia; this view is further supported by the experiments of Bernard and Barreswil,* who observed that the deleterious consequences of extirpation of the kidneys did not ensue in the dogs on which they operated, until the gastric juice was secreted with an alkaline reaction.

I have just become acquainted with the interesting experiments of Stannius,† who found that after extirpation of the kidneys, and even after the simultaneous injection of urea, urea itself could never be found in the secretions, or, at all events, in the gastric or intestinal juice or in the bile, but was detected in the sero-

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* Arch. gén. de Méd. 4 Sér. T. 13, p. 449.

† Arch. f. phys. Heilk. Bd. 9, S. 201—219.

On comparing the composition of the blood of the different *vertebrata*, we find in the first place, that amongst *mammalia* the *omnivora* exhibit the greatest number of corpuscles, and hence, also, the largest quantity of iron and of soluble phosphates. Fibrin also occurs in larger quantities here than in the blood of animals of other dietetic habits. The solid constituents of the serum also proponderate in the blood of these animals. The serum of the omnivora contains less salts than that of many other mammalia.

The blood of the *carnivora* generally contains nearly as many blood-cells as that of the omnivora: there is less fibrin but more fat in the blood of these animals than in that of the herbivora. The quantitative relations of the constituents of the blood vary considerably in the different species belonging to this class. A similar remark may be made regarding the blood of the *herbivora*, which on an average contains fewer blood-corpuscles than that of the carnivora, but the deviations from this rule are as great in the different species of this class as in the carnivora. We may, however, hope that a more careful study of the composition of the blood of these three groups of animals will enable us to detect more definite differences between them.

The blood of *birds* is rich in corpuscles, and stands next in this respect to that of the pig; it contains, however, more fibrin and fat, and less albumen, than that of the mammalia.

In the *cold-blooded vertebrata* the blood is poorer in corpuscles and richer in water than in the other *vertebrata*.

Although the *mollusca* possess a vascular system, consisting of arteries and veins and an aortic heart, their blood differs very considerably from that of the classes of animals immediately above them; being a white or bluish juice. C. Schmidt * found the blood of the pond-mussel (anodonta cygnea) colourless and slightly alkaline; it deposited a pale fibrinous coagulum, which on evaporation exhibited beautiful crystals resembling Gaylussite, and consisting of carbonate of lime and some carbonate of soda. The albumen was mostly combined with lime. This blood contained only 0·854% of solid constituents, and of these there were 0·033 of a fibrin-like substance, 0·565 of albumen, 0·189 of lime, 0·033 of phosphate of soda, chloride of sodium and sulphate of lime, and 0·034 of phosphate of lime.

E. Harless and v. Bibra† investigated the blood of the large

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* Zu vergleichenden Physiol. Mitau, 1846, S. 58—60 [or Taylor's Scientific Memoirs, vol. 5, p. 26.]

† Müller's Arch. 1847. S. 148—157.

Shell-snail (Helix pomatia) and that of certain Cephalopods (Loligo and Eledone), as well as of certain Tunicata (as, for instance, of some Ascidians).

The blood of the large Shell-snail contains, according to their investigations, 8·398% of organic, and 6·12% of mineral substances, there being 0·033 of oxide of copper in the latter. This blood is especially distinguished by assuming a blue colour on exposure to the air, in consequence of the access of oxygen, and again becoming colourless by the action of carbonic acid. Alcohol yields a colourless coagulum; ammonia removes the blue colour, which is restored by neutralization with hydrochloric acid. The blue pigment is precipitated by alum and ammonia, and is entirely destroyed at 50°. The blood of the Ascidians and Cephalopods presents the opposite relations in regard to colour to that of the large Shell-snail. It is not coloured blue either by oxygen or nitrogen, but carbonic acid converts it into an intense blue. Oxygen does not cause the entire disappearance of this colour; while ether and alcohol instantly communicate a blue colour to the originally colourless blood. Bibra found in this blood 4·7% of organic and 2·63% of mineral substánces, but no iron, although some copper.

I have made some experiments* on the blood of *insects*, and especially of the lepidoptera in their larva state. On making an incision into the skin of a caterpillar, on the abdomen, a transparent, thick, pale yellowish green juice exudes, which under the microscope discloses roundish cells without a distinct nucleus; the cell-walls appearing stippled like those of pus-corpuscles and having a diameter varying from $\frac{1}{350}'''$ to $\frac{1}{200}'''$. Dilute acetic acid does not change the cells, but the concentrated acid dissolves them. Caustic alkalies cause them to conglomerate into masses like most cells and even the yeast-globules, making them appear somewhat relaxed in texture, distorted and granular, so that they resemble granular cells. Hydrochlorate of ammonia does not change them. Besides these cells, we very frequently observe large roundish oval cells, having a distinct nucleus, and not unlike many of the pavement epithelium cells. These are not changed by acetic acid or the caustic alkalies. More rarely there occur pyriform, or spindle-shaped, and other irregularly formed cells. Fat-globules are always present in this fluid; they might be referred to the fat surrounding the stomach, if they did not likewise occur in the fluid of the dorsal vessels.

The intercellular fluid of the blood of insects assumes a dark

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* **Göschen's Jahresb. Bd. 2. S. 19.**

brownish green, or even black shade, when exposed to the air, and becomes turbid from the deposition of very fine molecular granules. It has a faint alkaline reaction, speedily develops ammonia on exposure to the air, and coagulates on being boiled, as well as on the addition of mineral acids or of a watery solution of iodine, into a thick white mass, without any separation of serum. It is also rendered turbid by water, and then resembles under the microscope a finely granular mass in which long threads are plainly discernible. Hydrochlorate of ammonia does not remove the turbidity, and the caustic alkalies or acetic acid remove it only slightly. Dilute acetic acid causes the fluid to gelatinize, and removes the blackish green colour, if it had previously been induced by exposure to the air. The caustic alkalies also convert the clear fluid into a colourless, tenacious jelly. Sugar may sometimes, but not always, be detected in this fluid. As caterpillars generate a larger quantity of fat within a short period than any other animals, their blood is also the richest in fat; amounting in one experiment to 27·5% of the solid residue. The fluid of the dorsal vessels in insects does not appear to differ essentially from the above-described juice, containing precisely the same elements with the exception of those nucleated cells which resist the action of acetic acid and the caustic alkalies.

The *blood of the arteries* differs from that of the *veins* in containing a smaller quantity of the solid constituents belonging to the blood-cells, which however contain relatively more hæmatin and salts than the cells of venous blood, but far less fat. The intercellular fluid of the arterial blood is richer in fibrin than that of venous blood. The serum of the former contains somewhat more water, and consequently less albumen; for if we compare the solid constituents of the serum of both kinds of blood in regard to their quantity of albumen, we shall find an equal amount of this substance in each. The case is different with the fats, extractive matters, and salts; for the first are considerably diminished in the arterial fluid serum, and even in its solid residue; and while the salts are but slightly augmented, the extractive matters are considerably increased in quantity. The arterial blood moreover contains relatively more free oxygen than the venous blood.

The *portal blood* differs in constitution according to the different stages of the digestive process; *during digestion*, when drink, as well as food, has been partaken of, it is rich in water and intercellular fluid; the number of blood-corpuscles is therefore small, the fibrin is slightly, and the fat very considerably augmented, while the albumen, extractive matters, and salts, are moderately *increased.* The fibrin during digestion remains the same as in the other vessels, but after the completion of that process it can readily be torn and forms only a loose diffluent clot.

Compared with the blood of the jugular veins, portal blood is poor in cells as well as in solid constituents generally; these cells are partly flocculent, are easily distorted, and soon become jagged after their removal from the body. They are richer in hæmatin and poorer in globulin than the cells of the blood of the jugular veins, but contain twice as much fat. The intercellular fluid contains a fatty fibrin, which, however, is inferior in quantity to that in the blood of the jugular veins. The serum contains on an average less solid constituents generally (especially albumen), but more fat, extractive matters, and salts. Biliary substances have not been shown to exist in portal blood, and sugar only seldom occurs.

The blood of the hepatic veins differs in constitution from that of any other vessels. *Compared with portal blood,* it is poor in water; for if we assume the solid constituents of the two kinds of blood to be equal, the amount of water in the portal blood will be to that in the hepatic venous blood during digestion, when little fluid has been taken, as 4 : 3, and after the completion of digestion not unfrequently as 12 : 5. The clot of hepatic venous blood is voluminous, and readily falls to pieces. While 100 parts of portal blood yield 34 of serum, 100 parts of hepatic venous blood yield only 15 of serum. Hepatic venous blood is far richer than portal blood both in coloured and colourless cells, the latter presenting every variety of size and form, and the former exhibiting heaps of a distinct purplish red colour. Their cell-walls are less easily destroyed than those of the blood of other vessels. While in the corresponding portal blood there are 141 parts of moist blood-cells for every 100 parts of intercellular fluid, there are in hepatic venous blood 317 parts blood-cells for 100 parts of the intercellular fluid. The cells of the latter blood are poorer in fat and salts; especially poor in hæmatin, or at least in iron, but somewhat richer in extractive matters. These cells have a greater specific gravity than those of portal blood (notwithstanding the diminished quantity of iron). On comparing the specific gravity of both kinds of blood with that of the serum, we find that the cells are lighter in relation to the serum in the blood of the hepatic veins than in that of the portal vein. The intercellular fluid of the former is far denser than that of the latter; it also contains a much larger quantity of solid constituents; but, on the other hand, it is either wholly deficient in fibrin, or only contains it in scarcely perceptible traces. While in the portal serum there are 8·4 parts of solid substances to 100 parts of water, there are 11·8 parts of solid matters to 100 parts of water in the serum of hepatic venous blood. When we compare the solid constituents in the serum of both kinds of blood, we find that hepatic venous blood contains less albumen and fat, and a much smaller quantity of salts; while the extractive matters, including sugar, are considerably increased. In the solid residue of the hepatic venous blood of horses, I found in three determinations (in which the alcoholic extract was excited to fermentation by means of yeast, and the sugar, $C_{12} H_{12} O_{12}$, was calculated from the developed carbonic acid) that the sugar was respectively 0·635, 0·893, and 0·776%; whilst in the residue of the corresponding portal blood I only once succeeded in detecting sugar, and then it only amounted to 0·055%.

The *blood of the splenic vein*, which has only been chemically examined, and compared with that of the jugular vein in horses and dogs by Béclard,* contains more water than the last-named kind of blood. The mean of 14 investigations in the case of dogs was 77·815%, the extremes being 74·630 and 82·681%. The corresponding jugular venous blood contained, on an average, 1·608% less water than the blood of the splenic vein. In two parallel investigations of horses' blood, the latter kind contained from 0·4 to 0·5% more water than the jugular venous blood. The blood-corpuscles are somewhat diminished, but the fibrin and the residue of the serum somewhat increased, in the blood of the splenic vein. Ecker† also found in the latter blood the cells containing corpuscles, discovered by Kölliker in the splenic juice. This was especially the case in the splenic venous blood of horses. From 1 to 5 corpuscles, or small yellow granules, were found enclosed in one capsule.

The *menstrual blood* contains no fibrin, as was shown by Jul. Vogel‡ in the case of a person suffering from prolapsus uteri, and has been recently confirmed by C. Schmidt.§ It yields a colourless but distinctly alkaline serum and a red deposit of blood-corpuscles; these are interspersed with numerous colourless cells, but there is no trace of the so-called fibrinous flakes. It contains about 16% of solid constituents.

Henle believes that the only reason that the menstrual blood

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* Gazette Méd. 1848. No. 4, p. 22, Janv.

† Handwörterb. de Physiol. Bd 4, S. 146.

‡ Wagner's Lehrb. d. Physiol. 2 Aufl. S. 230.

§ Diagnostik verdächtiger Flecke. Mitau u. Leipzig, 1848, S. 8 u. 41.

does not coagulate, is because each individual drop forms a distinct coagulum, and that consequently the sum of the drops must always constitute a tolerably fluid mass; but when examined under the microscope, menstrual blood does not exhibit any coagulated substance near or among the corpuscles. On the other hand, E. H. Weber found coagulated blood upon the mucous membrane of the uterus of a young girl, who had killed herself during the period of menstruation.

During *digestion*, the blood becomes richer in solid constituents, this increase extending with tolerable uniformity to the blood-cells and the plasma. The former gain in solid constituents, while they experience a relative loss of hæmatin (F. C. Schmid). The fibrin of the intercellular fluid is scarcely perceptibly increased, but it coagulates more slowly, and therefore more readily forms a crust upon the clot. Lastly, it is richer in fat than the fibrin obtained from the blood of fasting animals; the serum is denser, sometimes even exhibiting a milky turbidity from fat-globules and colourless blood-cells. It also presents a tolerably uniform proportional augmentation of fat, albumen, extractive substances, and salts.

Prolonged fasting and extensive losses of blood or of the other juices exert an action on the constitution of the blood precisely analogous to that of those substances which interfere with digestion or resorption and the formation of blood; as, for instance, many metallic salts, and especially preparations of lead, acids, &c. In these conditions, the number of the corpuscles diminishes in various degrees, while the plasma becomes more watery, (that is to say, poorer in albumen and other organic constituents,) but richer in salts. The blood has nearly the same constitution as in anæmic conditions.

In order to determine the influence exerted on the constitution of the blood by the abstraction of that fluid, numerous experiments have been made by Nasse on healthy animals, and by Becquerel and Rodier, Zimmermann, and others, on persons in disease. The results obtained showed that the specific heat, as well as the specific weight of the blood, was diminished; in colour, the blood was more brightly red; it coagulated more rapidly, but there was a less thorough expression of the serum, which exhibited a reddish or whitish turbidity. The red corpuscles, which were much diminished in number, showed a greater tendency to cohere. The colourless cells were increased in number (Nasse, Remak), and the quantity of water was considerably augmented; and at each venesection the blood became poorer in cells than in the solid constituents of the serum. The quantity of the fibrin was scarcely increased in healthy animals, and in disease it is altogether independent of the abstraction of blood. The blood-cells became poorer in globulin, and relatively richer in hæmatin (C. Schmidt).

These facts seem in some degree connected with the differences observed in the constitution of *different portions of blood taken at one and the same venesection* by Prevost and Dumas especially, but also by Becquerel and Rodier, and Zimmermann. After the loss of the first portion of blood (about 100 grammes), the solid constituents are in no case increased in the second portion, but on the contrary they almost always diminish with tolerable uniformity, while a third portion very frequently exhibits an increase of solid constituents when compared with the second (Zimmermann). This diminution of the solid substances depends upon the resorption of fluid, which obviously is owing to the absorption not of pure water, but of lymph, fluid exudations, and parenchymatous juice, which are lighter than the blood. The amount of absorption of water varies, however, very considerably in special cases. In Becquerel's experiments the quantity of water increased almost uniformly with each portion of blood, till it attained its maximum in the last that was drawn.

Inflammatory diseases constantly induce an increase of fibrin, when the inflammation is accompanied with fever. The number representing the fibrin is in general increased in the largest proportion in acute articular rheumatism and in pneumonia. A considerable increase of fibrin may be induced even where inflammation of a tissue is not very extensively diffused, as, for instance, in erysipelatous inflammations. In each individual disease the quantity of fibrin in the blood increases in proportion to the degree and duration of the inflammation. The increase of this substance is independent of the condition of the patient as to strength, and unconnected with the increase or decrease of the other solid constituents of the blood. Even in the most decided anæmia or hydræmia, the inflammation induces an augmentation of the fibrin. As the blood of persons who have died from acute cerebral diseases has never been found in a state of coagulation, it appears not wholly irrelevant to observe that in meningitis, &c., the blood removed from the living body has been found to be as rich in fibrin as it is in any other form of inflammation.

The number of the red blood-cells is decreased during the febrile inflammatory process, although not to any very great degree, unless the existence of other pathological processes has induced a simultaneous diminution of the whole mass of the blood-cells. In some cases scarcely any diminution of the blood-cells can be observed, although there may be a considerable increase of the fibrin.

The diminution of the solid constituents is in general proportional to the violence of the inflammation, and also to the quantity of exudations thrown off. Where there has been no great amount of exudation, the solid constituents are sometimes found to be augmented rather than diminished (as for instance in bronchitis). The diminution of the solid residue of the serum depends mainly upon the decrease of the albumen; for the salts in the serum are unaltered, and the fats, or rather the cholesterin, may be considerably increased.

We cannot at the present time attempt to decide whether the group of symptoms which accompany most acute diseases, and are designated as *fever*, are characterised by certain constant alterations in the relative quantities of the blood-constituents; but all investigations agree in showing that fever itself exerts neither an increasing or decreasing action on the vacillating amount of fibrin in the blood. The enquiries hitherto made, do not warrant us in deciding whether the admixture of the blood, which Becquerel and Rodier believe they have found to exist during the development of every acute disease, can be regarded as peculiar to fever. According to these authors, the blood presents at this time the following appearances: it is in general somewhat more watery than in its normal state; the corpuscles are slightly diminished in number, while among the fats, the cholesterin and the phosphorised fats are especially increased; the extractive matters and the soluble salts occur in normal quantity, while the phosphates are considerably augmented.

The same enquirers found that the blood-corpuscles, as well as the fibrin and the soluble salts of the serum, occurred in their normal quantity in simple *ephemeral* and *remittent fevers*, while the albumen was slightly diminished and the cholesterin increased.

In slight *intermittent fevers*, Zimmermann found that the fibrin was only increased in some few cases, being more frequently diminished, but it in general occurred in the normal quantity. Its increase appeared to stand in a direct relation to the duration of the fever. Becquerel and Rodier found the fibrin diminished in most cases of intermittent fever.

In *endemic intermittent fevers*, the blood-corpuscles are seldom diminished to any considerable degree, except in relapses, but are frequently increased in quantity. The fibrin is invariably augmented in inflammatory affections. The constituents of the serum increase when the disease presents an intermittent type, but decrease when the disease is characterised merely by remissions of severity. The diminution in the latter case mainly affects the albumen, while the salts of the serum are constantly augmented in quantity.

In *marsh-fevers* (malaria), the corpuscles are considerably increased (Salvagnoli and Gozzi, Luderer), while the fibrin, albumen, and fats, are proportionally diminished. A large quantity of cholesterin, as well as of bile-pigment, is in general found.

In *cholera* the blood is especially dense and viscid; and while the blood-corpuscles are relatively augmented, they are poorer in salts. The fibrin remains unaltered as to quantity; the serum is denser, poorer in water and salts, but relatively very rich in albumen; it also contains more potash salts and phosphates than normal serum, some urea, and an extractive substance by which urea is rapidly converted into carbonate of ammonia.

In *dysentery* the blood is poor in corpuscles. The fibrin is generally, although not always, somewhat increased. All the solid constituents of the serum are decreased, but especially the albumen. The salts, on the other hand, are considerably increased in quantity.

In *Bright's disease* the blood presents not only a considerable diminution in the number of cells, but likewise a great loss of the constituents of the serum. The cholesterin as well as the salts of the serum are, however, augmented, and the fluid almost always exhibits traces of urea, which in some cases is present in considerable quantity. Such blood contains on an average more fibrin than in the normal state, while it is only in inflammatory affections of the kidneys, that is to say, in its first stage, that there is any great augmentation of fibrin.

The *hydræmic blood* observed in different kinds of dropsy, is a very attenuated, pale, watery fluid; in coagulating it forms a very loose, infiltrated gelatinous clot. Its composition is very similar to that observed in Bright's disease, almost the only point of difference being the absence of urea. According to my experience at all events, this substance does not occur in hydræmic blood more than in dropsical exudations, unless in those cases in which renal affections are simultaneously present.

If by the term *anæmia* we understand a diminution of the quantity of blood in the vessels (*olichæmia* would, therefore, be a more correct expression, etymologically,) we can scarcely assert that the blood exhibits a perfectly identical or even an analogous composition in all conditions included under this designation, since the composition of the blood must necessarily correspond with the morbid process which preceded the diminution of the blood; for the properties which have commonly been ascribed to anæmic blood belong, properly speaking, to a hydræmic condition. We must, at all events, presume that the blood in anæmia depending upon excessive hæmorrhage, differs in composition from that exhibited in the anæmia which arises from large tumours, excessive mental labour, bad food, poisoning, &c. Experience teaches us, moreover, that the anæmia which follows carcinoma, typhus, hæmorrhages, and other losses of the juices, may easily pass into hydræmia, whilst in tuberculosis a hydræmic state of the blood is scarcely ever found to occur together with the corresponding serous exudations. Anæmic blood does not therefore indicate the existence of any special admixture of the blood. It is only in respect to the diminution of the coloured blood-cells that the composition of this blood corresponds with that exhibited in hydræmic and chlorotic conditions.

In *chlorosis* the blood forms a small solid clot covered with a bufly coat, and floating in a large quantity of clear serum. The corpuscles and the iron are both diminished either in a very small or in an excessive degree, without, however, standing in any definite relation to the intensity of the disease. The quantity of fibrin does not greatly exceed the normal average; the quantity of albumen is only increased relatively to the blood-cells, while the fats and salts remain entirely normal.

In the so-called *plethora*, the blood-corpuscles are always somewhat more numerous; the serum and the fibrin are both nearly normal, and the albumen of the liquor sanguinis rises only slightly above the mean average. Plethora seems to bear the same relation to spinal irritation as anæmia does to chronic spinal affections, the only difference being a greater increase of the solid constituents, and more especially of the blood-corpuscles, in the former.

The blood experiences no changes in *typhus*, which can justify us in terming this disease a dyscrasia. From the 5th to the 8th day, and therefore nearly as long as the continuance of the typhous exanthema, we find that the composition of the blood bears a great similarity to that exhibited in plethora, for the corpuscles are increased, as also are the solid constituents of the serum, and especially the albumen; even the fibrin is generally augmented at this period. From the 9th day of the disease the constitution of the blood assumes a totally different character; for at this period the blood becomes lighter, chiefly owing to a diminution of the corpuscles; the residue of the serum, however, diminishes daily through the entire duration of the disease, with a rapidity proportional to the intensity of the intestinal affection. The salts and extractive matters are relatively increased, rather than absolutely diminished. If typhus be not followed by any of its frequent sequelæ, or by the anæmia accompanying many of the epidemic forms of this disease, there is generally found to be an increase of the solid constituents about the beginning of the fourth or fifth week, which in some cases chiefly affects the blood-corpuscles, in others the solid substances of the serum, while occasionally even the quantity of the fibrin is augmented.

In *acute exanthemata,* there is a diminution of the blood-cells and a corresponding augmentation of the intercellular fluid. The serum is denser than usual, and its salts are far more augmented than the organic substances.

In *puerperal fever,* the blood varies according to the course and character of the morbid process (as indeed we observe in most cases of disease). There is a very considerable diminution of the corpuscles; the fibrin, especially in peritonitis, is much increased, but is soft and gelatinous, and almost always forms a crust. In most cases the solid constituents of the serum are considerably diminished (Scherer, Becquerel and Rodier); but sometimes they are increased (Andral and Gavarret); the extractive matters are considerably increased (Scherer); bile-pigment is occasionally met with (Heller); and not unfrequently free lactic acid (Scherer.)

In *pyæmia,* the fibrin is diminished, and the colourless blood-cells augmented; but more than this is not known, as the blood has not been carefully examined in this disease.

The blood has not been examined with accuracy in *scurvy,* and its composition has therefore been deduced principally from physical relations; thus, for instance, its imperfect coagulation led to the conclusion that it exhibited a diminution of fibrin, while other causes led in the same manner to the supposition that there was an augmentation of the salts. The few investigations of scorbutic blood which we possess, give but little idea of the true constitution of this fluid in the condition which we term scurvy.

The admixture of the blood in *tuberculosis* does not seem to differ greatly from the normal condition, for the modifications which it undergoes, appear, as far as our chemical investigations have enabled us to judge, to depend entirely upon the conditions which accompany this disease; thus, in inflammatory affections, the blood presents the same composition as in inflammations, while in those cases in which there is considerable loss of blood from hæmoptysis, or when profusely discharging intestinal ulcers or colliquative sweats are present, all the solid constituents of the blood, excepting the salts, decrease, as do also the blood-cells with even greater rapidity. Dropsy is not often associated with tuberculosis, but when this combination does occur, the blood presents the appearance of hydræmia.

The blood has not yet been very carefully examined in *carcinoma;* it is, however, worthy of notice that Popp, as well as Heller, and recently also v. Gorup-Besanez,* have discovered an increase of fibrin in carcinoma, even when unassociated with febrile affections. (It is certainly not shown whether the substance in excess was true fibrin.) The number of the blood-corpuscles is somewhat diminished. When dropsy is associated with cancer, the blood becomes hydræmic. As the solid constituents of the serum are not often abnormally increased, we cannot suppose that there is any serous or albuminous crasis in carcinoma.

Although we should naturally expect to find that the constitution of the blood undergoes a special alteration in *diabetes,* no such change has as yet been discovered; for, excepting its increased quantity of sugar, it presents nearly the same composition as normal blood. It is somewhat more watery, and contains less fibrin, but the blood-cells and solid constituents of the serum are only slightly diminished (v. Gorup-Besanez even found them increased). The serum sometimes exhibits a milky turbidity (Thomson).

The conception or idea of *scrophulosis* is as indefinite as that of *chronic rheumatism* and *arthritis;* and hence no scientific investigation of the blood in those conditions can be entered upon, for the blood must necessarily possess a different constitution when the scrofulous swellings of the cervical glands arise from ulcers on the pharyngeal mucous membrane, and when they depend upon tuberculous deposits. The constitution of the blood cannot be the same when uric-acid concretions are deposited in the joints, and when necrosis, osteoporosis, or osteosclerosis is established in consequence of periostitis. It has been asserted that the blood in scrofula is remarkable for its poverty of cells (Nicholson†), and

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* Arch. f. physiol. Heilk. Bd. 8, S. 523—525.

† Lancet. Nov. 1845, p. 451.

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* Arch. f. physiol. Heilk. Bd. 8, S. 523—525.

† Lancet. Nov. 1845, p. 451.

that arthritic blood is distinguished by the presence of uric acid and urea (Garrod*).

The immediate effect of the inhalation of ether seems to make the blood richer in water, poorer in blood-corpuscles, and strikingly rich in fat (Lassaigne,† v. Gorup-Besanez ‡). According to the numerous investigations of Gorup-Besanez,§ no distinct relation can be discovered between the *bruit* in the jugular veins and the chemical constitution of the blood. This sound may exist where there is an increase of all, or of some only of the solid constituents of the blood, or where they are diminished, or, finally, where there is a perfectly normal composition of the blood.

The *quantity of blood contained in the living body* has never been accurately determined, for the simple reason that the entire mass of the blood cannot be completely removed from the vessels and weighed; hence the determination can only be made approximately by indirect methods. Herbst endeavoured to calculate the quantity of blood in the vessels by the quantity required for the complete injection of the veins and arteries. But all who have made injections, or even carefully examined the injected subject, must feel that the estimate will be very uncertain when based upon such methods. Vogel,|| Dumas,¶ and Weisz,** have proposed but not practised other methods of determination. Valentin†† suggested the ingenious expedient of abstracting blood from an animal, whose weight was known, and after determining the solid constituents, immediately injecting a certain quantity of pure water into the veins, and then again taking blood and examining the solid residue with the greatest care. From the difference in the amount of the solid constituents in the two different kinds of blood, Valentin calculated the ratio of the weight of the whole blood to that of the body in dogs and sheep as 1 : 4½ in the former, and 1 : 5 in the latter. This method would afford sufficient accuracy if the walls of the blood-vessels were not more easily permeated by a thin than by a dense plasma,—if the whole mass of the juices in respect to the amount of water did not stand

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* London Medical Gazette. Vol. 31, p. 88.

† Gaz. Méd. de Paris. No. 11, 1847.

‡ Arch. f. physiol. Heilk. Bd. 8, S. 515–523.

§ Ibid. p. 532–543.

|| Pathol. Anat. des menschl. Körpers. Leipz. 1845, S. 59 [or English translation, p. 84].

¶ Chim physiol. et méd. Paris, 1848, p. 326.

** Zeitschr. d. k. k. Gesellsch. d. Aertze. Dec. 1847, S. 203—229.

†† Repert. der Physiol. Bd. 3, S. 281—293.

in such a relation to the blood that the state of the latter is almost immediately reflected in them (as indeed we see from the different composition of the separate portions of the blood in one and the same venesection, see p. 262),—if the blood did not continually give off water to the kidneys and other excretory organs,—and lastly, if the vessels were mere waterproof canals, without openings for the escape of the water, and for the importation of solid parts.

The discrepancies in the views of different physiologists in reference to the quantity of blood contained in the body of an adult man, are sufficiently obvious, when we remember that Blumenbach estimated it at 4 or 5 kilogrammes [from 8·5 to 11 pounds], and Reil at fully 20 kilogrammes [or 44 pounds]. In the present day the blood is generally estimated at 10 kilogrammes [or 22 pounds], which is equal to about the 8th part of the weight of the whole body. If I may advance the opinion at which I have arrived from experiments prosecuted on the bodies of two executed criminals, I should estimate the blood in the body of a young man as somewhat below the above quantity, namely, at from about 8 to 8·5 kilogrammes [or from 17·5 to nearly 19 pounds].

My friend, Ed. Weber, determined, with my co-operation, the weights of two criminals both before and after their decapitation. The quantity of the blood which escaped from the body, was determined in the following manner: water was injected into the vessels of the trunk and head, until the fluid escaping from the veins had only a pale red or yellow colour; the quantity of the blood remaining in the body was then calculated, by instituting a comparison between the solid residue of this pale red aqueous fluid, and that of the blood which first escaped. By way of illustration, I subjoin the results yielded by one of the experiments: the living body of one of the criminals weighed 60140 grammes, and the same body after decapitation 54600 grammes; consequently, 5540 grammes of blood had escaped. 28·560 grammes of this blood yielded 5·36 grammes of solid residue; 60·5 grammes of sanguineous water collected after the injection, contained 3·724 grammes of solid substances. 6050 grammes of the sanguineous water that returned from the veins were collected, and these contained 37·24 grammes of solid residue, which corresponds to 1980 grammes of blood; consequently, the body contained 7520 grammes of blood (5540 escaping in the act of decapitation, and 1980 remaining in the body); hence, the weight of the whole of the blood was to that of the body nearly in the ratio of 1 : 8. The other experiment yielded a precisely similar result.

We have no intention of asserting that such experiments as these possess extreme accuracy, but they appear to us to have the advantage of giving in this manner the minimum of the blood contained in the body of an adult man; for although some solid substances, not belonging to the blood, may be taken up by the water from the parenchyma of the organs permeated with capillary vessels, the excess thus obtained is so completely counteracted by the deficiency caused by the retention of some blood in the capillaries, and in part by transudation, that our estimate of the quantity of blood contained in the human body may certainly be considered as slightly below the actual quantity.

It is by no means decided whether fat men and animals contain less blood than lean ones, notwithstanding the experiments of Schultz* on fat and lean oxen (in the latter, he found an excess of 20 or 30 pounds of blood). When we enter upon the consideration of the animal processes, and especially the metamorphosis of matter, we shall treat in detail of the sources from which the blood flows, its progressive and regressive formation, both in relation to its individual constituents and collectively, and of its general physiological import; for the blood is the centre round which the general metamorphosis of animal matter revolves, and in which it is perfected. As we have already considered the origin and metamorphosis of the chemical constituents of the blood, in the first volume, it only remains for us here briefly to notice the mode of development and the destination of its morphological elements, although these questions may be regarded as belonging more especially to histological physiology.

The investigations of the most distinguished physiologists of the present day render it highly probable that there is more than one *seat of formation of the colourless blood-cells.* They are, undoubtedly, for the most part, formed in the chyle, and they are likewise produced, as has been before observed, in the liver; at all events, under certain conditions: but their formation, or at all events their development and growth, are not confined to any one definite locality, but proceed in the vessels of very different organs. H. Müller† and Kölliker‡ have recently devoted special attention to the development of the colourless blood-cells in the chyle,—a subject that had already been very fully considered by several earlier observers, especially J. Müller, E. H. Weber, Schwann, Henle, and

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* System der Circulation. Stuttgart, 1836.

† Zeitschr. f. rat. Med. Bd. 3, S. 204—278.

‡ Ibid. Vol. 4, pp. 142—144.

Reichert. We find that the chyle contains numerous morphological elements, whose supposed significance as embryonic blood-corpuscles, and whose different forms in the course of their development, have led physiologists to very different views. H. Müller, who is opposed to the cell-theory of Schleiden and Schwann, thinks that the origin of these bodies from the chyle-plasma may, according to his observations, be explained somewhat in the following manner:—In the minutest lacteals there appear minute clots (solid corpuscles without a distinct cell-membrane), which are separated from the chyle, and occur as dense granules, with a viscid matter connecting them together. From these minute clots, the rudiments of the cell-wall and the nucleus are developed by a certain alteration in the chemical substrata. The nucleus appears most granular in the more recent formations, since it has been formed by the conglomeration of the insoluble and denser granules, whilst the cell-wall was being condensed into a membranous capsule. Since even at the termination of the thoracic duct we meet with minute clots in which cell-formation is only commencing, it is not improbable that their conversion into true cells—that is to say, into colourless blood-cells—is effected within the blood itself; in like manner, the first tendency towards the formation of such cells may also take place within the blood from its plasma. Müller draws attention to the fact, that most of the colourless cells of the blood contain tripartite nuclei, resembling also in this respect pus-corpuscles. We also find that the blood always contains cells with a simple nucleus (like the mucus-corpuscles of healthy mucous membranes); and on the other hand, that the chyle contains cells with a multiple nucleus. A slight difference in the chemical constitution of the chyle-plasma on the one side, and of the blood- or exudation-plasma in (suppuration) on the other, may perhaps be the cause of a simple nucleus in the former, and of a fissured or multiple nucleus in the latter. Kölliker strongly opposes Müller's views, and is of opinion that Schwann's theory is strictly applicable to the development of the colourless blood-corpuscles. He found at the commencement of the lacteals, but never in the thoracic duct, nuclei which were either free or surrounded by granules, and young cells with walls which almost touched the nucleus, and were very fragile. He most distinctly maintains the existence of nucleoli. Besides this origin of the lymph-corpuscles in the minutest lacteals, Kölliker also assumes that they are further augmented in the intermediate vessels, although he leaves it undecided whether this increase is effected by endogenous formation or by subdivision. The same observer distinguishes larger and smaller lymph-granules in the thoracic duct, and is of opinion that the latter only are converted into blood-corpuscles, whilst the larger gradually dissolve in the blood.

The view that the blood-cells of the embryo originate in the liver, was long since advocated by Reichert,* and recently by several physiologists, and more especially by E. H. Weber† and Kölliker.‡ Weber showed that in the spring the liver of frogs assumes a totally different colour, while at the same season this organ is the seat of an active formation of new blood-cells. Gerlach,§ whose observations have been supported by those of Schaffner,|| has, however, very recently endeavoured to prove that the spleen is the chief factory for the blood-cells; but the admirable chemical investigations of Scherer seem far more to corroborate the view opposed by Kölliker, and subsequently by Ecker,¶ that the blood-corpuscles are for the most part destroyed in the spleen. This much, at all events, seems certain, that the formation of the blood corpuscles is not limited to definite organs, for blood-corpuscles appear in the germinal area of the embryo before the formation of vessels and glands. In the area vasculosa, blood-corpuscles and vessels are formed from cells which, according to Reichert, can in no way be distinguished from one another. There can be no doubt, therefore, that the coloured blood-cells may proceed from the colourless ones; but, as yet, it remains undetermined whether such is always the order of formation, and how this mode of development is effected.

If we were to regard the colourless blood-corpuscles as merely a transition stage of formation of the coloured corpuscles, their significance and physiological importance would at once be defined; but however ephemeral their existence in the blood may be, we cannot wholly deny their participation in the chemical metamorphosis of matter, more especially as many of these bodies do not appear to be converted into coloured corpuscles. They are vital cells, maintaining an active interchange of matter with the blood-plasma, and cannot therefore be wholly without influence on

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* Entwicklungsleben im Wirbelthierreich, S. 22.

† Zeitschr. f. rat. Med. Bd. 4, S. 160.

‡ Ibid. Vol. 4, pp. 147—159.

§ Ibid. Vol. 7, pp. 75—88.

|| Ibid. Vol. 7, pp. 345—354.

¶ Ibid. Vol. 6, pp. 261—265.

the general composition of the blood and the metamorphosis of the animal tissues.

With reference to the chemical phenomena accompanying the morphological transition of colourless into coloured cells, we only know that hæmatin is gradually developed within them, and hence we must content ourselves with a brief reference to the views held by recent physiologists regarding the morphological process; omitting all notice of the older hypotheses.

The once generally accepted view that the red blood-corpuscles are formed from the nuclei of the lymph- and chyle-corpuscles, by the disappearance of their walls, has found no advocates in recent times. H. Müller, on the other hand, adopts the view that the colourless cells are directly converted into the red blood-corpuscles, and believes that the small lymph-corpuscles which occur in the thoracic duct owe their origin to the loss of their fluid granular contents, and that thus the capsule approximates more closely to the nucleus, whilst all their contents disappear so entirely in the blood, that the membrane comes in contact with, and constitutes the actual investment of the nucleus. The corpuscle is then flattened in an analogous manner to the nucleus, and appears concave, while the nucleated vesicle imbibes red pigment and thus becomes formed into a perfect blood-corpuscle. The chemical behaviour of the cell-wall of the corpuscles seems however opposed to this view, and there are many other reasons unfavourable to its adoption.

According to Kölliker, the most probable view is that which assumes that the smaller kind of chyle-corpuscles is converted by the disappearance of the nucleus and the absorption of pigment into the true blood-corpuscle; he advances the following grounds in support of this view: (1) The similarity of size in the smaller chyle-corpuscles of the thoracic duct and the red blood-corpuscles; (2) the perfectly identical behaviour of the capsule of these chyle-corpuscles and of the wall of the blood-discs towards physical and chemical influences; (3) the faintly yellow colour of these chyle-corpuscles with an entirely colourless nucleus; (4) the flattening, although in a less degree than in fully developed blood-corpuscles; and (5) the nuclei of the smaller chyle-corpuscles are entirely different from the blood-corpuscles.

To these three theories regarding the transition of colourless into coloured corpuscles Gerlach has added a fourth, which is principally founded on the occurrence of cells containing blood-corpuscles in the Malpighian corpuscles of the spleen and in the liver of the embryo. According to him, the coloured blood-corpuscles are formed within the colourless ones, so that the latter stand in the relation of parent-cells to the former. But as this subject belongs less to physiological chemistry than to pure histology, the present remarks must suffice until we are able to bring chemistry to our aid in explaining the progressive and regressive development of the blood-cells.

As yet we know very little of the manner in which the *blood-corpuscles* act in the living blood, the objects they fulfil or the results of their chemical metamorphoses. But our deficiency in positive knowledge has here been liberally supplied by hypotheses, whose value we will briefly consider. As might be expected, the discovery of these peculiar molecules in the blood led to that false and illogical application of the word "life" which even now is not wholly banished from physical physiology. The very vagueness of the term "life" served as a cloak for everything that did not readily admit of being referred to physical or chemical agencies. The molecules of the blood were supposed to be endowed with individual vitality like the infusoria, for which they were even mistaken by some observers (Eble and Mayer), in proof of which assertion it was maintained, according to Czermak, Treviranus and Mayer, and still more recently by Emmerson and Reader, that they exhibited a spontaneous motion. Very recently, moreover, one of our most distinguished chemists has been erroneously led by his experiments to believe in a peculiar vital activity of the blood-corpuscles. Dumas could not resist advancing the assertion that the blood-corpuscles possess a certain respiratory activity which may occasionally be reduced to actual asphyxia. It will be a sufficient refutation of this view, if we mention that Dumas was led to this conclusion merely by making the well-known observation that blood-cells, when treated with neutral alkaline salts, cohere when at rest, assume a darker colour and begin to be decomposed at a moderate temperature; while this alteration occurs at a later period, when the blood which has been acted on by salts is frequently shaken. Dumas thought that the access of oxygen, brought about by shaking the blood-corpuscles, caused them to retain their vitality for a longer period; but when they are shaken with nitrogen or hydrogen gas, they do not sooner become dark than when they are shaken with atmospheric air; hence it is merely the motion which retards the cohesion and further decomposition of the blood-cells. In order to avoid misconception, we would, however, observe in reference to the vitality of the blood-cells, that if by the term "life" we mean simply a group of physical and chemical agencies, having reference to morphological progressive and regressive development, vitality can no more be denied to the blood-corpuscles than to any other animal or vegetable cell.

An opinion long prevailed that the blood-corpuscles took up oxygen in the lungs and gave it off in the capillaries, the view being based upon the bright red colour of the blood in the lungs, and its darkness in the capillaries. These cells were in fact regarded as carriers of oxygen. Henle refutes this view by observing that we might, with equal justice, also term them water-carriers, since they show themselves no less capable of absorbing the smallest additional quantity of water than of taking up oxygen and carbonic acid; for they absorb water, and again give off a portion of it, in a state of vapour, in the lungs; the gases through whose assumed chemical action this function of the cells was supposed to be derived, could only exert a mechanical influence on the form, and therefore on the colour of the blood-cells. This opinion derived great probability from Mulder's careful investigation of hæmatin, which was found to be perfectly indifferent to gases, and likewise from the above named inquiries of Nasse, Henle, Scherer and Bruch, who have shown the influence exerted on the colour of the blood by the alterations in the form of the cells. There are, moreover, two other facts which appear to render this supposed function of the blood-cells exceedingly doubtful, if not wholly untenable; in the first place, Marchand could not obtain the slightest trace of carbonic acid in blood through which oxygen had been passed after the removal of all the gases; the conversion of oxygen into carbonic acid cannot therefore take place within the cells themselves. Another observation, made by Hannover, speaks, however, still more strongly against the usually adopted view; for this observer found that chlorotic patients, whose blood is often exceedingly deficient in coloured blood-cells, exhaled in like periods of time as much carbonic acid as healthy women. Hence we might be disposed to believe with Henle, that there is no intimate relation between the corpuscles and the gases of the blood, if there were not two important grounds, supported on facts admitting of only one interpretation, which are in favour of the view according to which the blood-cells possess the capacity of absorbing oxygen. The first of these grounds rests upon the observation already referred to, that neither the intercellular fluid nor the serum alone has the power of absorbing more than a small quantity of oxygen, while the cell-containing blood exhibits a very strongly marked capacity for absorption: a fact that speaks so strongly in favour of the function of the blood-cells, that it requires no further exposition. The second ground supporting the idea of the capacity of the blood-cells for absorbing gases, is that diluted hæmatin or copiously watered blood which contains only some few recognizable corpuscles, whose contents (the hæmatin, &c.) are for the most part in a state of solution, is still susceptible to the action of carbonic acid and oxygen; the alteration of colour cannot possibly depend in this case on alterations in the form of the blood-corpuscles. The hæmatin of Lecanu and Mulder is not the same as that contained in the fresh blood-cells; although the solution of the blood-cells very probably does not play the part ascribed to it, the recently dissolved hæmatin must yet participate with the blood-corpuscles in the capacity for absorbing gases. Marchand's experiment simply proves that the blood-corpuscles are not capable of generating carbonic acid by their own unaided power, or when removed from the body and brought in contact with oxygen. With respect to Hannover's view, independently of the circumstance that it admits of several modes of interpretation, it by no means overthrows the opinion that the blood-cells possess this capacity; for if a person having few blood-cells exhales as much carbonic acid as another whose blood is richer in corpuscles, it does not follow from this that the production of carbonic acid directly depends upon the blood-corpuscles, but seems rather to show the very reverse. The blood-cells, in all probability, absorb most of their carbonic acid after they reach the capillaries, and they are obviously able to take up a larger quantity than they commonly convey to the venous blood: thus 80 or 100 corpuscles of chlorotic blood may absorb the same quantity of carbonic acid as that which is generally absorbed by 120 corpuscles of healthy blood in the capillaries; these 80 cells may therefore, in like manner, exhale as much carbonic acid in the lungs as the 120. Then, moreover, the intercellular fluid exhibits a greater capacity for dissolving carbonic acid than oxygen, and it would not therefore require the co-operation of the blood-corpuscles to convey to the lungs the carbonic acid transuded into the capillaries. We therefore consider the view which ascribes to the blood-corpuscles the function of absorbing oxygen, and giving it partially off in the capillaries, not only to be uncontroverted, but to be completely proved.

The question here arises, whether the oxygen is only mechanically taken up by the blood-cells or loosely combined with them, or whether it is chemically united with some of the individual constituents and thus directly gives rise to the formation of carbonic acid in the capillaries. Both these modes undoubtedly occur; for the greater part of the oxygen absorbed in the lungs is only mechanically taken up by the corpuscles, or is brought to the capillaries in a slightly combined form, as is clearly proved by the experiments of Magnus, Marchand, and others; but it would be very singular if the blood-cells, which are so susceptible to external influences—as, for instance, to chemical agents—and which undoubtedly manifest an active metamorphosis of matter, should remain wholly unaffected by oxygen. This is, however, by no means the case, as we learn from direct observations. We have already shown, and purpose making still more evident by a special reference to analyses, that the difference in the chemical constitution of the arterial and venous blood-corpuscles can scarcely be explained except by the assumption of a chemical action of the oxygen upon the individual organic constituents of the blood-corpuscles in the lungs. We would here only observe, that we found the mineral substances and the hæmatin augmented in the blood-corpuscles after the inspiration of oxygen, whilst the organic substances, and more especially the fats, were considerably diminished. This incontestible fact can scarcely be explained, excepting by the supposition that it is only the mineral substances and the hæmatin which increase in weight by the absorption of oxygen, whilst the organic substances, and more especially the fats, are either destroyed by oxidation, and their products of decomposition transferred to the intercellular fluid, or at all events they undergo a considerable diminution of weight by the formation of water and carbonic acid. No one, however, can seriously believe that the blood-corpuscles swim unchanged, like mechanical molecules, from the capillaries of the lesser to those of the greater circulation.

Although we are not yet able to express the function of the blood-cells in exact chemical equations, and therefore cannot comprehend their precise physiological import, we may yet, from the facts at our disposal, form some general opinion in reference to the purpose of their existence in the blood. The blood-corpuscles are cells having special contents, whose existence cannot be conceived on physical grounds without a simultaneous and continuous metamorphosis of matter. Their activity must correspond to the menstruum in which they are suspended, and to all the relations generally in which they occur in the living body. We must, *a priori*, conclude that each recent animal cell in the healthy blood is, under given relations, metamorphosed into blood-corpuscles, precisely as we see the primary type of the animal cell, the chyle-corpuscle, converted into a blood-cell; for it is an incontrovertible proposition in physiology, that like conditions acting on like substrata, must give rise to identical results. If, however, the formation of a cell depend upon the medium surrounding it, its subsequent activity can only be developed in relation to this medium; hence the blood-cells and the plasma must stand in a constant reciprocal relation to one another, precisely as the yeast-cells do to the fermenting mixture. It remains, however, for future inquiries to determine the metamorphoses which result from this reciprocal action. As far as we are at present able to form an opinion on this subject, we think we shall not be deviating very widely from the truth, if we regard the blood-cells as organs, that is to say, as laboratories, in which the individual constituents of the plasma are prepared for the higher function of aiding in the formation and reproduction of the tissues. As soon, however, as we attempt to specify the individual constituents of the plasma, we lose ourselves in a labyrinth of hypotheses. Thus, for instance, some observers have conjectured that fibrin was elaborated from albumen, which is *possible*, in so far as fibrin appears to be a substance ready elaborated for deposition in the tissues, but *improbable*, since we also find in some cases that the fibrin is increased in an extraordinary degree in blood which is very poor in corpuscles (chlorosis).

The blood-corpuscles, like all other cells endowed with vital activity, have a definite period of existence. This limited duration has been regarded by some philosophical inquirers as a specific property of living beings, as if every physical or chemical process must not in like manner have a definite period of duration limited by a commencement and a termination. No one can doubt that the activity of the blood-corpuscles has its boundary, and that they perish, although the mode and course of their gradual destruction yet remains a mystery. All we know is, that in our microscopico-chemical investigations, the cells of the same blood vary in the length of time during which they can resist chemical agents, and hence it is conjectured that the more easily decomposed cells, which, moreover, generally exhibit greater intensity of colour, are the older, and that those which are not easily acted upon, are paler, and appear in their granular contents to present the rudiments of a nucleus, are of more recent origin. We have no certain knowledge of the length of time that an individual cell continues to exist. The observation made by Harless, that a frog's blood-corpuscles entirely disappear after nine or ten alternations of oxygen and carbonic acid, would enable us to form an average estimate of the period of their duration, if it were not that both these substances were employed in the experiment in a state of purity, whilst in the lungs the blood-corpuscles are only acted upon by atmospheric air containing about 4$\frac{0}{0}$ of carbonic acid. We may presume from a comparison of the blood taken in repeated venesections, that the period of duration or existence of the red corpuscles is not very short; for the circumstance that the blood continues for several days after a moderate venesection to be poor in corpuscles, and even exhibits a great deficiency of these bodies for a prolonged period after repeated venesections, certainly proves that their regeneration is not effected with great rapidity. If, however, they are slowly regenerated, as appears to be the case, judging from the copious supply of colourless cells in the circulating fluid after severe losses of blood, they cannot have a very short existence, for otherwise the number of the coloured cells would not so far exceed that of the colourless corpuscles.

The question, whether the *blood-corpuscles are disintegrated at one definite spot*, has not yet been decided with any certainty. It was generally supposed by the earlier observers, that the destruction of the blood-corpuscles was effected by the alternating action of oxygen and carbonic acid, as well as of different salts and other substances, this action being gradually continued throughout the whole course of the blood-vessels, and their products also undergoing a gradual solution. As the arterial blood has been found to be poorer in corpuscles than the venous, some support seemed to be afforded to the view that the older blood-cells were principally destroyed in the capillaries of the lungs by the access of oxygen; but as it has been only proved that the weight of the sum of the blood-cells is diminished, and not that their number is lessened, we are by no means compelled to assume that the blood-cells are destroyed in the arteries; and it would even appear probable, on many grounds, that the weight of each cell is diminished by respiration, but not that the whole number is lessened. There seems, however, to have been a disposition to connect the disintegration of the blood-cells with one definite locality, and Schultz more especially designated the liver as the organ in which this process was effected. F. C. Schmid's more accurate investigations of the portal blood and of the coloured cells contained in it, which differ from those of other blood, appear indeed to afford a more exact foundation for this hypothesis. We have already spoken at length of the constitution of the portal blood and of its relation to the hepatic function, in the chapters on "bile" and on "the blood," and from our comparative analyses of the portal and hepatic venous blood, we are led to the conclusion that the liver ought rather to be regarded as an organ for regenerating the blood-corpuscles than as the seat of their destruction, although we will not deny that blood-corpuscles, which have usually been regarded as cells in an advanced state of development, are conveyed from the splenic to the portal vein. On the other hand, during digestion we found only normal blood-corpuscles in the blood of the portal vein. Schultz's view cannot, therefore, be received without a certain reservation. An opinion has been lately advanced by Kölliker, and still more recently by Ecker, from the histological investigation of the spleen, and more especially of the Malpighian bodies, that this organ which was previously held to be the seat of the formation of blood, and indeed is still regarded as such by Gerlach and Schaffner, is in fact the principal seat of the solution and complete disintegration of the blood-corpuscles. While such contending views prevail among the most trustworthy histologists, we should not venture to give the preference to either of these opposite theories, if chemical analysis did not here, as in so many cases, come to the aid of histological inquiry. Scherer has made a very admirable investigation of the spleen, which has led to several important discoveries; the chief result of which is, that in the splenic juice there occur all the most remarkable transition stages of the products of decomposition of nitrogenous and albuminous matters, and of the blood-pigment itself. It seems highly probable from this investigation that the spleen aids in the destruction of those blood-corpuscles which are no longer able to accomplish their proper functions. We will, however, defer the fuller consideration of this hypothesis, which results from the simplest induction, till we treat of the chemico-physiological nature of the spleen,—having, moreover, already far exceeded the limits originally prescribed to the present chapter on the blood.

CHYLE.

The chyle presents various physical properties which differ with the condition of the animal (as for instance, whether it is fasting or has been lately fed), the part of the chyliferous system from whence it has been procured, and the nature of the food that has been taken. It commonly forms a milky, opalescent, yellowish white or pale reddish fluid with a faint animal odour, a somewhat saline and mawkish taste, and a very faint alkaline reaction. Like the blood, it coagulates in nine or ten minutes after its removal from the chyliferous system; the coagulum, which contracts in from two to four hours, is much smaller than that of the blood, and is very soft, friable, and sometimes merely gelatinous. When exposed to the air, it generally assumes a somewhat light red colour, if it had previously been yellow. This is especially observable in the chyle of horses. The serum of the chyle, although clearer than fresh chyle, still in general retains some degree of turbidity; when merely diluted with water, it seldom becomes more turbid, but when boiled, it becomes of a milky white colour, and commonly deposits a few minute clots. Acetic acid often induces a turbidity (Nasse*); on evaporating the fluid filtered from the albuminous coagulum, the surface appears covered with a colourless transparent membrane (albuminate of soda). The chyle-serum does not coagulate when treated with ether, but is rendered clearer. A dirty yellowish white, cream-like stratum is formed between the ether and the chyle-serum.

According to Tiedemann and Gmelin, as well as according to Nasse, the chyle is almost colourless and transparent in birds, amphibia, and fishes; while, according to J. Müller, Gurlt, Simon, Nasse, and my own observations, it is of a deeper red colour in horses than in any other animals which have hitherto been examined with reference to this subject. Nasse found the chyle of cats of a perfectly milky whiteness. During digestion the chyle is in general extremely turbid; at other seasons it forms a faintly opalescent fluid, which only exhibits a reddish colour in the thoracic duct.

The chyle that has been collected during digestion is very rich in morphological elements, since it exhibits, as a highly plastic fluid, the most varied stages of cell-formation. Hence a great variety of molecules have been distinguished in it, and the pro-

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* Handwörterbuch der Physiologie. Bd. 1, S. 235.

ducts of different stages of development have received the name of chyle-corpuscles. (J. Müller,* Schultz,† R. Wagner,‡ Henle,§ Nasse,|| Arnold,¶ Kölliker,** Herbst,†† H. Müller.‡‡)

As a more detailed description of these molecules falls rather within the province of histology than of chemistry, we refer our readers to the works of the above-mentioned observers, limiting ourselves here to a notice of the most important points in reference to the microscopical investigation of the molecules of the chyle. In the first place, chyle which has been taken from the minutest lacteals during digestion, exhibits *extremely minute granules,* which cover the field of view like a thin veil. These granules, which have been especially examined by H. Müller, and recognized to be fat-granules surrounded by a protein-like capsule, remain unaltered on the addition of water, but flow together and form the ordinary fat-globules when the chyle is treated with acetic acid or dilute caustic potash. A similar result is observed when the chyle is suffered to dry and the residue is again dissolved in water. Most observers agree in the opinion that *no true fat-globules* are generally contained in the fresh chyle of animals, although they have frequently been found in human chyle; this may, however, be owing to the circumstance that the chyle which is usually taken from the body some time after death, may already be partially decomposed, and may therefore be acted upon by putrefaction, somewhat in the same manner as by the potash.

In addition to these fine molecular granules, the chyle, more especially at the origins of the vessels, contains also *coarser granules* which are grouped into masses and appear to be held together by means of a hyaline substance (H. Müller), and distinct, sharply-defined *nuclei* with nucleoli, which are in some cases covered with individual granules (Kölliker).

It has generally been assumed that there are special *chyle-corpuscles* which are the distinguishing constituents of the chyle; but these bodies do not actually differ from the lymph-corpuscles

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* Handb. d. Phys. Bd. 1, S. 235 [or English Translation, 2nd Ed., vol. i. p. 281.]

† System der Circulation. Stuttg. 1836, S. 45.

‡ Beitr. z. vergl. Physiol. Bd. 2, S. 56.

§ Allg. Anat. S. 421—471.

|| Handwörterb. der Physiol. Bd. 1, S. 226.

¶ Anatomie, S. 260.

** Entwicklungsgeschichte der Cephalopoden. Zürich, 1844, S. 50, and Zeitschr. f. rat. Med. Bd. 4, S. 142—147.

†† Lymphgefässsyst. u. seine Verrichtungen. Gotting. 1844, S. 603.

‡‡ Zeitschr. f. rat. Med. Bd. 3, S. 239.

or the colourless blood-corpuscles, being distinguished from the latter only in this, that they represent different stages of the development of these cells. They present considerable variety of size and form, exhibiting in some cases a distinct, and in others an indistinct nucleus, and sometimes even a cleft nucleus which frequently remains indistinct until it is treated with water, and hence these corpuscles appear in the chyle itself like mere faintly translucent vesicles. It is worthy of notice that many of these bodies have frequently a magnitude of 1-200th of a line in the lacteals of moderate calibre, whilst the size of those in the chyle of the thoracic duct seldom exceeds 1-250th or 1-350th of a line.

We have already noticed their chemical relations in speaking of the colourless blood-corpuscles, and we purpose again reverting to the subject under the head of pus-corpuscles.

If the search be conducted with care, *coloured blood-corpuscles* may always be found in the chyle of the thoracic duct, although they are not present in large quantities.

In order to obtain the largest possible quantity of fresh chyle, the animal should be killed from two to five hours after feeding, either by strangulation or pithing, the thoracic cavity opened, and the thoracic duct tied immediately before its entrance into the subclavian vein. After a short time the duct will be filled with chyle, and will appear distended or as if it were injected. It must then be carefully dissected into the abdominal cavity as far as the receptaculum, and the contents discharged with care (in order to avoid all admixture of blood), either by means of a fine trochar or by simple incision. A greater quantity of chyle may be obtained by laying open the thoracic portion of the duct and suffering the chyle to flow from the incision; but the precipitous flow of chyle in the freshly killed animal may possibly give rise to a more abundant flow of lymph and aqueous fluid, so that the chyle may not possess a perfectly normal character.

In reference to the *chemical constituents* of the chyle, we may observe that they entirely correspond with those of the blood; and hitherto only very slight, or even wholly unimportant differences have been observed to exist between the plasma of the blood and the chyle. This admits of a ready explanation, for an accurate chemical analysis is only practicable in the case of the chyle of the thoracic duct, which not only resembles the blood far more closely than does the chyle of the smaller vessels, but which has even taken up blood that is already coloured, together with blood-corpuscles, from the lymphatics of the spleen.

Next to the undissolved molecules of the chyle, whose chemical constitution lies even further beyond the range of our inquiries than that of perfect blood-cells, the *fibrin* has the principal claim on our attention. It differs from that of the blood in generally exhibiting a less considerable contractility, and the somewhat gelatinous consistence to which pathological anatomists have applied the term "fibrin infiltrated with serum." Like the fibrin in many morbid exudations, it is occasionally redissolved some hours after its coagulation, especially when the surrounding temperature exceeds the usual mean. It does not often exhibit the fibrous texture of solidly coagulated blood-fibrin under the microscope, but dissolves very readily in diluted alkalies and organic acids, and, after being digested for a short time, in a solution of nitre or even of hydrochlorate of ammonia. It may be completely precipitated from the acetic-acid solution by hydrochlorate of ammonia, and again almost perfectly separated from this solution by acetic acid. I found only 1·77% of strongly alkaline ash in chyle-fibrin which had been duly deprived of its fat, well washed, and dried. Like the fibrin of the blood, the chyle-fibrin always contains some of the above-named morphological constituents of the chyle, and is therefore even richer in fat than the blood-fibrin, but it very seldom happens that the fibrin of the chyle encloses in its coagulation all the elements which were suspended in the intercellular fluid; and on this account the serum of the chyle is in general clearer than the original chyle, although it always retains some degree of turbidity, or at all events of opalescence.

In the serum of the chyle *albumen* is also the preponderating solid constituent. This albumen has been regarded as imperfectly developed (Prout), owing to the circumstance that it coagulates on being heated, and is at the same time precipitated to a certain degree by acetic acid. Independently of the illogical character of the argument which can assume the existence of a chemically imperfect substance,—and we might just as rationally assume that malaria is a more perfect carburetted hydrogen than olefiant gas, or the reverse,—every one who has read the observations in page 332 of vol. i., must at once conclude that the only difference presented by the albumen arises from its being combined with more alkali in the chyle than in normal blood; and this, moreover, is confirmed by direct investigation, at least in the chyle of the thoracic duct of horses. The chyle-serum is not rendered turbid by strong dilution with water; when boiled, it does not so much form coherent flakes as a milk-white, opaque fluid; and it becomes covered on evaporation by a colourless membrane. The aqueous extract of the residue of the chyle exhibits a strongly alkaline reaction, and the solution may be rendered turbid by neutralising it with acetic acid. After this turbidity has been removed by a more copious addition of acetic acid, ferrocyanide of potassium gives rise to a considerable precipitate. The aqueous extract of the residue of the chyle presents great turbidity on being boiled with hydrochlorate of ammonia, as well as on the addition of nitric acid. The albumen, after being thoroughly washed with water, alcohol, and ether, was found to yield on incineration 2·068% of mineral constituents, including a considerable amount of alkaline salts, which effervesced on the addition of acids. The supposed presence of casein in the chyle, instead of being proved, seems therefore to be rendered very improbable.

It would be an important point if we could show that the *peptones* of the albuminous substances in the food are present in the chyle, but from our ignorance of the necessary reagents, this question cannot at present be decided by direct investigation. As the chyle contains from 2·5 to 3·0% of non-coagulable substances which are only soluble in water, and consist of a large proportion of albuminate of soda and mineral salts, it is at all events improbable, to say the least, that peptones should be present in the chyle discharged from the thoracic duct of the horse; and hence the question, whether the peptones are elaborated in the mesenteric glands into albumen and fibrin, still continues wholly undecided.

Our microscopical and microscopico-chemical investigations prove that *fat* is contained in large quantity in the chyle, and even show with some degree of probability that the chyle contains a considerable quantity of non-saponified fat in the smaller lacteals, whilst in the thoracic duct the proportion of saponified fat preponderates. I was unable by any method to obtain a crystallizable fat from the saponified or non-saponified fats of the chyle of the horse; and other observers have stated that they could only discover a greasy and tallow-like fat, although they may not always have attempted to detect the fat-crystals by the aid of the microscope.

Some authors profess to have found *sugar* in the chyle; others could not discover this substance. Trommer* believes he has detected its presence in the chyle of horses by means of his own sugar-test, but it is well known that many causes concur in destroying the practical value of this test. Thus, for instance, the

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* Ann. d. Ch. u. Pharm. Bd. 39, S. 360.

chyle contains albuminate of soda, which passes into the alcoholic extract, and exerts a disturbing influence on the reaction; this substance may yield the most beautiful blue solution with sulphate of copper and potash, and at all events, after prolonged boiling, may give a yellowish red precipitate without the chyle containing a trace of sugar. The substance which is formed is the albuminate of the oxide of copper, investigated by Lassaigne, which on prolonged boiling with potash likewise precipitates suboxide of copper. I have never been able to detect any sugar in the chyle of horses fed on bran, but the presence of this substance could be determined with certainty in the case of horses which I had fed for a considerable period on starch or highly amylaceous food, by applying the method indicated in vol. i., p. 284 and with due attention to all the precautions specified, and also by the fermentation-test. It would appear, therefore, as if sugar only passed into the chyle in appreciable quantities where there was an excess of it in the intestine.

Biliary constituents cannot be detected in the chyle by any method hitherto attempted. (See pp. 72 and 90.)

I have determined with certainty the presence of *alkaline lactates* in the chyle, at least after feeding animals with amylaceous food. (See vol. i., p. 95.)

The chyle is very rich in *alkalies*, which are combined partly with albumen, partly with lactic acid, and partly with fatty acids; hence the aqueous solution of the ash exerts a strongly alkaline reaction, and effervesces with acids.

Alkaline sulphates do not exist pre-formed in the chyle, but occur in its ash. Thus, for instance, if the aqueous extract of the solid residue of the chyle, after being treated with alcohol and ether, be carefully neutralised with acetic acid, evaporated, and again dissolved in water, filtered, and finally treated with a salt of baryta after being previously acidified by nitric acid, there will not be the faintest trace of turbidity nor any subsequent deposition of the slightest sediment.

We find no trace of *sulphocyanides*, which might possibly have passed into the chyle with the saliva conveyed to the intestine; at all events the salts of peroxide of iron do not impart any perceptible redness to the alcoholic extract of the chyle.

The *alkaline phosphates* occur only in very small quantities even in the ash of the chyle produced from vegetable food.

The *chlorides of sodium and potassium* are present in the chyle in large quantities. Salts of ammonia, and especially the hydrochlorate, have also been supposed to occur in the chyle; we would here simply refer to vol. i., p. 452, where the reasons are given which have led to the adoption of this erroneous view. The efflorescent appearance of the chlorides of sodium and potassium, as seen under the microscope on examining the evaporated spirituous extract, has led to their being mistaken for hydrochlorate of ammonia; but if such appearances were due to the latter substance, there would be no crystals of phosphate of soda, but simply the very easily recognisable crystals of phosphate of ammonia and soda. Moreover, bichloride of platinum precipitates the potassium-compound, but not the ammonium-compound, from the spirituous solution. We have, further, explained in vol. i., p. 160, that the occurrence of the octohedral and tetrahedral forms in which the chloride of sodium is so frequently observed under the microscope in evaporated animal fluids, and frequently also in the chyle, is no evidence of the presence of urea.

It is very difficult to determine whether or not the serum of the chyle is free from *iron*, like that of the blood; Reuss and Emmert,* Vauquelin,† Rees,‡ and Simon, believe that they have ascertained the presence of iron in the serum of the chyle, and they regard it as more loosely combined than in the blood, that is to say, they suppose that it is united with phosphoric acid or other substances which do not impede the ordinary reactions of the salts of iron. We do not, however, consider ourselves justified in concluding from our own observations, or from those of the above-named chemists, that the serum of the chyle contains iron, because, as it can never be obtained perfectly free from coloured, or at all events colourless cells, the iron that is found may very probably belong to these cells. No one, indeed, would maintain that there is an entire absence of iron in the serum of the chyle, any more than in that of the blood; for the iron must necessarily pass from the plasma of the chyle into the cells, returning in the blood to the intercellular fluid from the cells which are undergoing the process of destruction: but the iron does not appear to constitute an integral constituent of either fluid.

Little remains to be noticed in reference to the *method of analysis* to be pursued in the quantitative investigation of the chyle, after the remarks we have already made in treating of the analysis of the blood and of the animal juices generally. It will

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* Reil's Arch. Bd. 8, S. 147—218.

† Ann. du Museum nation. d'hist. nat. T. 18, p. 240.

‡ London Medical Gazette, Jan. 1841.

be obvious from the properties of its constituents which have been already noticed, that the quantitative determination of the cells, of the fibrin, and of the albumen in the chyle, must be very uncertain, for we do not possess any means by which we can retain the chyle-corpuscles and other molecules on the filter, or which will enable us to compute their weight. These bodies are distributed, together with the other molecules suspended in the chyle, through the fibrin and albumen: and as the fibrin of the chyle in general coagulates very imperfectly, the lymph-corpuscles are less completely enclosed than in the fibrin of the blood, and the molecules which remain suspended in the chyle are therefore enclosed by the coagulated albumen. The sinking capacity of the chyle-corpuscles is so inconsiderable, that the coagulated albumen often reddens when exposed to the air, in consequence of the enclosed pigment-containing cells, in the same manner as the fibrin of the chyle. We can, therefore, only arrive at a moderately approximate determination when, as in the case of the blood, we abstract from the solid residue of the chyle-clot the fibrin determined by whipping. Hence, that which is supposed in ordinary analyses to be fibrin, is very often scarcely half composed of this substance, in reality consisting, in addition to these molecules, of a very large quantity of fat which has been inadvertently suffered to remain, as is frequently the case in analyses of the blood. The precautionary rules which we have already laid down for the determination of albumen (vol. i. pp. 338-340), apply to the investigation of chyle more, perhaps, than to that of any other animal fluid. All the directions indicated for the determination of the fat in the blood, refer with equal force to the chyle. The ordinary rules hold good for the determination of the individual extracts and the various mineral constituents. The older analyses, however, to which we might look for assistance, are scarcely able to yield us any purely physiological results, in consequence of their having been prosecuted without the benefit of those aids to analysis which we possess in the present day. The following observations give the results of the *quantitative investigations* of other observers, in addition to my own.

The *quantity of water* in the chyle of horses fluctuates, according to the investigations of different enquirers, between 91 and 96%; this chyle contains, therefore, as a minimum 4, and as a maximum 9% of *solid constituents*. Nasse found 90·57% of water in the chyle of a cat.

The number of *cells, cell-nuclei,* and other *molecules* contained in the chyle must vary with the nature of the food that has been taken, but these relations, as we have already observed, do not at present admit of being determined. Except during the period of digestion, the chyle contains few cells and in almost all respects resembles the lymph.

The quantity of *fibrin* in human chyle has not been determined; but attempts have frequently been made to ascertain the amount of this substance in different animals, and especially in horses, although this has seldom been accomplished without an admixture of corpuscles and fat. In the chyle of the horse Tiedemann and Gmelin* found from 0·19 to 0·7%, and Simon,† from 0·09 to 0·44%; I found a coagulum which was very rich in cells amount to 0·495%, while the fibrin, as free from cells as possible, determined from the same chyle, amounted to 0·301%. Tiedemann and Gmelin found from 0·17 to 0·27% in the dog, and from 0·24 to 0·82% in the sheep; Rees found 0·37% in the ass, and Nasse, 0·13% in the cat.

Tiedemann and Gmelin found from 1·93 to 4·34% of *albumen* in the chyle of horses, and I found 3·464% as the mean of several analyses in the chyle of horses fed upon bran, and 3·064% in that of horses fed on starch.

Tiedemann and Gmelin found 1·64% of *fat* in the chyle of horses, Simon from 1·001 to 3·480%, while I found from 0·563 to 1·891%; Rees found 3·601% in the chyle of the ass, and Nasse 3·27% in that of the cat.

Simon found from 8·874 to 9·892% of *extractive matters free from salts* in the solid residue of the chyle of horses, while I found 7·273% in that of horses, when fed upon bran, and 8·345% when fed upon starch.

The chyle of horses contained, according to Simon, from 6·7 to 7·3% of *soluble salts*, (determined from the ash,) while according to my own researches, it yielded 7·45% when the animals were fed upon bran, and 6·784% when they were fed upon starch. The chyle of the cat contained, according to Nasse, 9·4% of soluble salts, of which 7·1 was chloride of sodium.

The chyle contains about 2% of *insoluble salts*. The mineral constituents of the solid residue of the chyle amount, therefore, on an average to 12%, of which from 9 to 10% are soluble salts.

Numerous observations have been made on the influence which the *nature of the food* exercises on the constitution of the chyle,

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* Verdauung nach Versuchen. Bd. 2, S. 75.

† Med. Chem. Bd. 2, S. 241-244 [or English translation, vol. i. pp. 354-359].

but these results, or rather the conclusions deducible from them, differ considerably. This much, however, seems certain, that the chyle is somewhat poorer in solid constituents after prolonged fasting or where the food has been scanty, and that it then contains a much smaller quantity of fat, so as to appear only slightly turbid, but not milky. It has been generally maintained, that the chyle becomes richer in fat after animal food, but this is only the case where the nutriment has consisted of flesh, bones, milk, or other fatty kinds of animal substances; for Tiedemann and Gmelin found that the chyle of dogs was rendered only faintly turbid, when these animals were fed on albumen, fibrin, casein, and gelatin. All observers agree in the opinion that the chyle becomes milky and very rich in fat when the food has been of a fatty kind. According to my observations, non-nitrogenous substances do not produce any decided augmentation of fat in the chyle. No definite conclusions can be drawn from the enquiries and opinions of observers in reference to the influence exerted by the nature of the food on the quantity of albumen and fibrin in the chyle, for these substances owe their origin partly to transudation from the blood in the mesenteric glands, and partly to the lymphatics of the spleen, while moreover the chyle of the thoracic duct is the only kind which has been accurately examined with a view of ascertaining its quantitative relations.

Nor can we attach any great weight to Millon's* elementary analyses of the chyle and blood of dogs which had been fed on different kinds of food; at all events we cannot concur with that observer, when he believes himself justified in concluding that the special purpose of the lacteals is not the absorption of fats only, but also of other nutrient substances in an equal degree.

The chyle undergoes many alterations during its passage from the lacteals of the intestines through the mesenteric glands to the thoracic duct. We have already spoken of the diversity existing in the morphological elements in the different parts of the chyliferous system, in reference to the fibrin which, according to Tiedemann and Gmelin, occurs in the smaller lacteals either in very small quantities, or is entirely absent; we only know that its quantity appears gradually to augment during the passage of the chyle through the glands. A similar observation applies to the albumen, which, according to the same observers, is conveyed in large quantities to the chyle in the glands, so that this fluid appears to increase in density in proportion as it approximates to the receptaculum chyli. Fat is the only substance which seems to be

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* Compt. rend. T. 29, p. 817—819.

gradually diminished during the passage of the chyle to the blood, and this may be owing to its participation in the formation of cells, that is to say, of chyle-corpuscles, which are very rich in fat, and partly to its transition into a state of saponification, as we may judge from the quantity of the alkaline salts of the fatty acids present in the chyle of the thoracic duct.

No direct observations have as yet been made concerning the *pathological relations* of the chyle.

We cannot regard the question of the *quantity of chyle* which enters the blood in a given time, as satisfactorily settled. Cruikshank* assumes the quantity of chyle which is hourly mixed with the blood to be 4 pounds. His calculation rests upon an observation of the rapidity of the motion of the chyle in the mesentery of a dog, which he found to be four inches in a second, and hence he assumed a similar rate of velocity in the thoracic duct. But independently of the untenability of the latter position, the rapidity of the motion of the chyle in the lymphatics of the mesentery depends upon many different relations, which, from their variable character, can scarcely be adequately appreciated in observations made during vivisection. Magendie, who endeavoured to determine the quantity of the chyle by opening the cervical portion of the thoracic duct of well-fed dogs, and observing the quantity which flowed in a given time, found that half an ounce escaped in five minutes, which was at the rate of six ounces in the hour. Bidder, who has made similar experiments on dogs that had been previously strangled, arrived at nearly similar results ; but unfortunately, as this observer remarks, such experiments scarcely warrant us in drawing any definite conclusion. If, for instance, as Vierordt† observes, the ascent of the chyle be arrested by cutting the thoracic duct, which is one of the most efficient causes of its motion, it must not be forgotten, that this operation may be followed by too abundant a discharge ; for here, as in the analogous but more strongly marked case of the blood, there will necessarily be an afflux of juices from all sides, which must increase in an extraordinary

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* [Lehmann refers in a foot-note to p. 78 of Ludwig's translation of Cruikshank's "Anatomy of the Absorbing Vessels" as his authority for this assertion. All that Cruikshank says is: "The chyle in the lacteals of the mesentery of dogs, in some of my experiments, evidently run through a space of four inches in a second, which is twenty feet in a minute." 1st Ed. Lond., 1786, p. 29. In neither his first nor his second edition (published in 1790) does he attempt to determine the quantity of the chyle.—G. E. D.]

† Arch. f. phys. Heilk. Bd. 7, S. 281—285.

degree the *vis a tergo*, however small it may be, by which the chyle is propelled. The lymph will at all events flow more abundantly, rendering the result of the enquiry so uncertain as to prevent any proper solution of the physiological question concerning the quantity of the newly-formed and elaborated nutrient matter which passes through the chyle-vessels.

Vierordt proposes the following method for computing the quantity of the chyle which passes into the blood of an adult in 24 hours:—As 100 grammes of dry nitrogenous matters are daily consumed by an adult man, and as the chyle contains about 4% of such matters, the quantity of chyle daily formed will amount to 2½ kilogrammes, or about 5 pounds.* Vierordt himself observes that this calculation does not admit of a comparison with those of the earlier inquirers, because the lymph mixed with the chyle and flowing from the lymphatics, is not included in the computation, and because the quantity cannot be even approximately computed, owing to our uncertainty regarding the quantity of the lymph. The quantity of albumen which the chyle receives in the mesenteric glands, is excluded by Vierordt in his calculation, because he regards it as too small to require notice. To those who believe with Vierordt, that nitrogenous nutrient matters can only reach the blood through the lacteals, his mode of calculation may serve as an index of the quantity of the chyle; but all who concur with Frerichs and other observers, in assuming that the peptones are resorbed by the stomach and intestinal canal through the veins—an opinion which appears to be borne out by many circumstances—will necessarily attach more weight to the direct observations of Magendie and Bidder, than to Vierordt's calculation.

On the other hand, Vierordt would have approximated more nearly to the truth, if, instead of selecting the nitrogenous constituents, he had based his calculation on the quantity of fat in the chyle and the amount of fat which was daily resorbed in the intestinal canal. We know from Boussingault's† admirable experiments on ducks, that these animals are not able to take up more than 19·2 grammes in 24 hours, however rich in fat their food may be. We are, therefore, led to presume that there may be a similar limit to the resorption of fat in other animals. From numerous experiments on cats Schmidt, Bidder, and Lenz‡ have indeed convinced

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* [The kilogramme = 2.2 pounds avoirdupois; hence 2½ kilogrammes = 5½ pounds.—G. E. D.]

† Ann. de Chim. et de Phys. 3 Sér. T. 19, p. 117—125.

‡ De adipis concoctione et absorptione. Dorp. Liv. 1850, p. 62—79.

themselves of the correctness and general applicability of Boussingault's observation; for they found that cats weighing 1000 grammes were able to take up from 0·6 to 0·9 of a gramme of fat in one hour, the surplus being carried off with the excrements. It is far more probable that all the resorbed fat should reach the blood through the lacteals, than that all the protein-bodies should pass into the chyle; and hence we shall probably obtain a nearer approximate number for the chyle which passes hourly into the blood, by adopting the amount of fat in the chyle of cats as the other basis of our calculation. Nasse, as has been already observed, found 3·27% of fat in the chyle of a cat; now, if no lymph flowed into the chyle, and if we assume that lymph contains some, although not much, fat (for Tiedemann and Gmelin found only traces of fat in the contents of the thoracic duct of fasting horses), and if it were shown that the chyle does not actually lose any fat in the mesenteric glands (this substance only becoming saponified), and that all the fat of the chyle of the thoracic duct has originated directly from the intestinal contents, cats weighing 1000 grammes would pour 22·9 grammes of chyle into the blood in one hour (supposing that they absorbed 0·75 of a gramme of fat in the same time), or 549·6 grammes of chyle in 24 hours. But as this would be more than half their weight, it is very improbable that this is the correct quantity. If we assumed six hours as the period during which true chyle passes into the blood, a cat weighing 1 kilogramme would daily elaborate 137·4 grammes of chyle. These calculations, more especially when they are extended to the human organism, are, however, far too uncertain to afford any stable support to our future inquiries into the mechanical metamorphosis of matter, for there exist innumerable relations by which the result of such calculations may be completely modified. It would carry us too far from our subject were we to enumerate all these relations; we will, therefore, simply remark that probably a large quantity of fat is not conveyed from the chyme to the lacteals, but is resorbed by the veins, for how otherwise could the portal blood of animals be almost twice as rich in fat during the process of digestion as in the fasting condition? (See p. 247.)

We cannot entertain any doubt as to the *origin* of the chyle, since nature itself has clearly manifested its source to us. Certain questions here present themselves as to the mode in which the individual constituents pass into the lacteals, and the alterations which they undergo within these vessels. The lacteals originate in the axis of the villi which are spread over the whole of the small intestine, and present small club-like dilatations. The lacteals are surrounded at their origins by vesicles or cells which appear as if imbedded in an indistinct fibrous mass; while nearer to the exterior and to the peripheral investment of cylindrical epithelium covering the intestinal villi, there lie the trunks of the minute blood-vessels, which communicate together by means of a very fine net-work of capillaries. According to E. H. Weber,* there is a layer of round cells situated immediately below the epithelium, which are collapsed during fasting, and inflated like well-filled vesicles during the process of digestion. All observers concur in the opinion that each individual particle of cylindrical epithelium participates in the process of resorption, and is filled with a granular substance which causes its distension, and in some cases even a slight distortion. It is, however, more especially and almost exclusively during digestion that this layer of round cells appears under the epithelial investment; some of these cells being then filled with a clear, transparent, faintly yellow fluid, others with a granular substance. Thus we often find a cell of this kind filled with limpid fluid situated on the apex of an intestinal villus, and close by it another cell of equal size, filled with granular emulsive matter.

Besides numerous observations on animals in relation to this point, I remember noticing this appearance most strikingly and distinctly in the intestinal villi of a decapitated criminal, in whose examination E. H. Weber had permitted me to take part. The microscopical preparations made by Weber at the time have kept so well, that they still fully testify to the accuracy of his observations, and show that the structures in question are neither epithelial cells filled with fat (as was conjectured by Frerichs) nor fat-globules merely adhering to the surface of the villi. The distortion of the cells which Frerichs was also unable to detect, may likewise be easily recognised in these preparations.

The limpid contents of these clear globules, which are probably the oscula of the intestinal villi, according to the views of the older physiologists, can from their refractive power scarcely be anything but *fat*, and this leads us at once to the hypotheses regarding the resorption of fat by the intestinal villi. R. Wagner† assumes that the solid neutral fats must be fused by animal heat previously to their resorption, whilst the fluid fats are resorbed unchanged. In order to explain

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* Müller's Arch. 1847, S. 399. [We may also refer the reader to Professor Goodsir's remarks on this subject in his "Anatomical and Pathological Observations," pp. 5-10.—G. E. D.]

† Lehrb. d. spec. Physiol. 3. Aufl. 1845, S. 263. Anm. 3.

the passage of the fats into the intestinal villi, Wagner has assumed that some portions of the intestinal canal are intended solely for the absorption of the fats, and others only for taking up the aqueous fluid. We should, however, rather be disposed to assume with Lenz* that certain cells in each intestinal villus are solely destined for the absorption of fat,—a mode of explanation which would be especially convincing to the chemist, who is accustomed to separate fatty from aqueous fluids by means of a filter saturated in one case with water, and in the other with oil. If we constantly observed (as we might often do) that the apex of each intestinal villus exhibits one vesicle more conspicuous than others for its size, and filled with a clear, strongly refractive fluid, together with another equally prominent vesicle, filled with granular matter, we should the more readily be led to the adoption of this hypothesis, since it affords an explanation of the view advanced by Boussingault, and confirmed by Bidder and Schmidt, that the absorption of fat from the intestine is confined within definite limits. Lenz adopted a very ingenious method for the further support of this hypothesis, which, however, did not prove so satisfactory as might have been desired. He injected butter, that had been coloured with alcanna pigment, into the stomachs of cats, and killed the animals some hours afterwards. Most of the cells were found to be filled with yellowish fat, but this appearance could not afford any decisive explanation of the subject under consideration. However ingeniously this experiment was conceived, its frequent repetition was scarcely calculated to yield perfectly reliable results, for the fat would certainly become mixed in some places with the aqueous fluid, and as it would have to penetrate through several cells before it reached the smaller lacteals, it would enter those vessels mixed with the watery fluid; and this admixture would likewise go on in the villi of the cells surrounding the origins of the lacteals. If the cells filled with fat, and situated on the periphery of the villi and at their outer extremities, did not differ so strongly from the others, it would be illogical to attempt to explain the occurrence of a process in the interior which has been regarded as improbable at the surface, the relations existing in both being very nearly identical. Here, however, these relations are somewhat different, for we find some cells containing fat, and others filled with an albuminous fluid, appearing to be closely compressed together This pressure may easily exert a modifying action on the permeability of the delicate cell-membranes, in the same manner as we

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* Op. cit. p. 86—89.

find that on pouring an oily, emulsive, watery fluid on a filter, which has been completely saturated with water, oil will penetrate at some spots. The extreme comminution of the fat in the intestinal canal, which is occasionally observed to take place under ordinary relations, through the agency of the bile and the pancreatic juice, is by no means necessary; at all events, Schmidt and Bidder found that in animals into whose intestine pure fat had been conveyed after the exclusion of the bile and pancreatic juice, the lymphatics of the mesentery were as completely filled with milky chyle, as they usually appear to be after the use of fatty nutriment, when there is a free access of these glandular secretions. We cannot, therefore, assume the occurrence of an extreme comminution of fat in the aqueous fluid at the surface of the villi; but as the separate cells of the villi rapidly fill, and soon begin to exchange and blend their contents, the repetition of the experiment made by Lenz can scarcely afford any decisive results; for although the colouring by alcanna may cause the cells to be more conspicuous under the microscope than they would otherwise appear, the cells which were originally filled only with an aqueous fluid would speedily acquire the same hue, in consequence of their being partially permeated by coloured fat. We must, moreover, confess that we are as yet unable to explain, from any known physical facts, the relations of transudation occurring in the cells. We will here merely refer to the rapidity with which the cells are frequently filled with granules of fat in certain pathological conditions, and to the still greater rapidity with which they are emptied—processes which have been most carefully studied by Virchow. A dehiscence of the cells may very probably occur only at individual points, and in such a manner, that the cell recovers its original integrity after the discharge of the superfluous substance. But these are all questions for whose further elucidation we must look to future physico-physological inquiries.

We find more free and much less saponified fat in the small and intermediate lacteals than in the thoracic duct; and hence we are led to assume that a gradual saponification of the fat takes place in the mesenteric glands, where the chyle is undoubtedly brought in closer contact with the blood; this process being effected by means of the alkali of the latter fluid. A portion of the free fat is undoubtedly employed in the cell-formation which then ensues, but we can scarcely hazard a conjecture as to the chemical mode in which those metamorphoses are effected, which the fats themselves undergo in this process. But as it is certain that more alkaline salts of the fatty acids exist in the chyle of the thoracic duct than in that of the smaller lacteals or even than in the blood, these saponified fats cannot originate from the lymph that is mixed with the chyle, or from the plasma of the blood, but must rather be owing to saponification within the lacteals themselves.

The two following questions especially force themselves upon our notice, in considering the origin of the *albuminous substances* contained in the chyle:—1. Is the fibrin found in the chyle formed within that fluid, or does it originate in the intercellular fluid transuded from the blood? and 2. Does the *albumen* reach the intestinal villi in its perfect state, or are the absorbed peptones elaborated into albumen within the cells of the villi and in the lacteals? In respect to the latter of these questions, we have already (at pp. 104 and 123) indicated the grounds which have led us to the view that the peptones are not converted into albumen in the intestinal canal itself, notwithstanding the incontrovertible facts which have been advanced by Frerichs in favour of the opposite opinion. The system of cells through which the absorbed albuminous substances (and consequently the peptones, according to our view) have to pass before they can enter their proper vessels (the lacteals) and the abundant net-work of capillaries enclosing these cells, appear to us clearly to indicate that these substances have here still to undergo important changes, whose final product can scarcely be anything else than true, coagulable albumen containing alkali. It has further been found that the chyle after its passage through the mesenteric glands, is richer in albumen than it previously was; and this augmentation is solely referable to the absorption of blood-albumen in the glands. In proportion to our certainty on these points, so much the more probable it becomes that the augmentation of the albumen, at all events in part, depends upon the complete metamorphosis of the peptones into coagulable albumen.

In regard to the second question, we must remain undecided between the opposite results of Prout* and of Tiedemann and Gmelin,† as to whether the chyle contains true *fibrin* before its passage through the glands, or whether the coagulum observed by the former chemist, did not consist of fat, cells, and other albuminous matters. If the plasma actually passes from the blood into the lacteals, which, indeed, cannot be doubted, it would seem most probable that the whole of the small quantity of fibrin which is contained in the chyle originates from the blood or from the lymph.

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* Annals of Philos. Vol. 13, pp. 12 and 265.

† Op. cit., p. 157.

This view is further supported by our observations (in vol. i. pp. 360-364) regarding the origin and the physiological importance of the fibrin. The soft, friable character of the chyle-fibrin has usually been regarded as affording a proof that it is first produced from albumen in the chyle, and that hence it appears there in such an imperfectly formed state. But we have already remarked in reference to the albumen, that the idea of greater or less perfection in regard to chemical substances is altogether inadmissible; we can only speak of an imperfect development when we treat of morphological objects. The reason why the fibrin in the chyle often (although not always) separates in this peculiar form is in no way connected with its being imperfectly elaborated from albumen; it solely depends on the character and chemical composition of the fluid from which the separation takes place. In diseased blood and in pathological exudations, we likewise observe that the fibrin separates in the same loose, friable, and sometimes even diffluent form as from the chyle; indeed, we are able to induce this loose, friable coagulation of the fibrin by artificial means, as, for instance, by diluting the plasma with water, by the addition of alkalies, &c. On these grounds, it seems far more probable that the fibrin of the chyle is due to the blood-plasma and lymph which have been absorbed into the lacteals, than that perfectly formed albumen should be here oxidised into fibrin.

With regard to the other constituents of the chyle, they are already formed in the chyme, and pass unchanged into the lacteals; it is singular that sugar, which I only found in such very small quantity in portal blood, is also only present in extremely small quantity, or is altogether absent, in chyle. This circumstance may be, in some degree, explained by the consideration that the conversion of starch into sugar in the intestine usually proceeds only very slowly, and that hence only very small quantities enter the lacteals and blood-vessels.

We have already noticed the development of the *morphological elements of the chyle* within the lacteals, in our remarks on the origin of the colourless corpuscles (see p. 273).

It has been maintained by several of our leading authorities, that *hæmatin* occurs in solution in the chyle-serum, and that hence it must be formed in the chyle; but independently of the circumstance that a similar relation to that in the case of the fibrin may also hold good here, that is to say, that it may owe its origin to the blood-cells of the splenic lymphatics, it cannot have been possible for these chemists, with the aids at their command, to decide with certainty whether the hæmatin that was found, did not belong to the red corpuscles of the chyle. At all events, I have been unable to detect any dissolved hæmatin in the chyle-serum from the thoracic duct in horses, which is most commonly of a red or cinnamon colour, and holds in suspension true hæmatin-containing blood-corpuscles; if, however, decomposition has commenced in the chyle, hæmatin will then be found in the plasma in consequence of the disintegration of the blood-corpuscles.

LYMPH.

The lymph forms a colourless or yellowish fluid, which is only red if blood-corpuscles happen to be mixed with it; it is sometimes transparent, sometimes slightly turbid or opalescent, of a faintly saline taste and mawkish animal odour; its reaction is usually alkaline; it coagulates in from four to twenty minutes after its discharge from the lymphatics; it then forms a gelatinous, trembling, colourless coagulum, which gradually contracts more firmly, and encloses a large number of the so-called lymph-corpuscles; in relation to the serum this coagulum usually occupies only a very small space.

Besides fat-globules and nucleus-like formations, we especially notice amongst the *morphological elements* the true lymph-corpuscles which, however, do not essentially differ from mucus- and pus-corpuscles. In lymph that has been carefully collected, we only find blood-corpuscles when the fluid has been obtained from the lymphatics of the spleen or from animals that have been starved to death. (H. Nasse.)*

There are many difficulties in the way of our *obtaining* pure lymph; it is sufficient to mention that, except in the very largest animals, it is often extremely difficult to find and dissect the lymphatics, and that even in the most favourable cases we cannot avoid an admixture of blood and fat, on cutting into the vessel and allowing its contents to discharge themselves. Hence recourse has generally been had to accidental cases, and lymph has been analysed which escaped spontaneously in consequence of a wound or from a true lymphatic tumour. By the method

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* Handwörterb. der Physiol. Bd. 2, S. 363—410.

described by J. Müller,* we can in a short time obtain from frogs a very considerable quantity of lymph, which, however, usually contains a slight admixture of blood; we make a crucial incision through the skin of a frog's thigh, and dissect a portion of skin, above and below, from the subjacent muscles; from this wound there flows such a quantity of lymph, that if we amputate the thigh, we often obtain more lymph than blood. Fishes usually have tolerably large lymphatics in the lower part of the orbit, and we may readily collect their lymph by opening the orbit from below and then cutting the absorbents.

The simplest method of obtaining a large quantity of lymph would be by cutting the thoracic duct of animals which had been for a long time deprived of food; but I agree with Nasse in considering this method as unfit for yielding a lymph sufficiently genuine and pure for chemical analysis.

The *chemical constituents* are, in general, very similar to those of the blood without red corpuscles. The spontaneously coagulating substance of the lymph is perfectly identical with the *fibrin* of the blood; like ordinary fibrin, it is converted, by digestion in a solution of nitre, into an albuminous substance coagulable by heat and precipitable by acetic acid. As in the case of the chyle, it is impossible here also to determine its quantity very accurately, since we are unable to separate it completely from cell-formations. In human lymph (obtained in cases of disease or injury), Marchand and Colberg† found 0·52% and L'Heritier 0·32% of fibrin, while in the lymph of the horse from 0·04 to 0·33% has been found (Reuss and Emmert,‡ Gmelin,§ Lassaigne,‖ Rees,¶ Geiger and Schlossberger**). J. Müller found that frogs which had been starved during the winter, yielded a lymph perfectly free from fibrin, while on the other hand, Nasse found that the lymph of frogs which had been kept in a heated room, still coagulated.

The *albumen* of the lymph has the same general properties as that of the blood; Geiger and Schlossberger have, however, recorded the singular result that the albumen from the lymph of a horse, although it exhibited no reaction with vegetable colours,

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* Handb. der Physiol. des Menschen. 4 Aufl. Bd. 1, S. 203 [or English translation, 2nd Ed., vol. 1, p. 278].

† Pogg. Ann. Bd. 43, S. 625.

‡ Allg. Journ. d. Ch. Bd. 3, S. 691.

§ A. Müller, Diss. inaug. Heidelb. 1819, p. 59.

‖ Recherches physiol. et chimiques etc. Paris, 1825, p. 61.

¶ Phil. Mag. Feb. 1841, p. 156.

** Arch. f. phys. Heilk. Bd. 5, S. 392—396.

did not coagulate on boiling, but that on evaporation there was a membrane formed on the surface of the fluid as if a strongly alkaline albuminate of soda had been present; this lymph-serum was not rendered turbid by acetic acid, unless after being thus acidified it was boiled; as no coagulum was induced by rennet, it was obvious that no casein was present; moreover this serum was not coagulated by ether. In human lymph the albumen has been found to vary from 0·434 (Marchand*) to 6·002% (L'Heritier), and in that of the horse from 1·2 to 2·75%.

In the ash of the albumen of the lymph, even after repeated extractions with water and spirit, Nasse found an extraordinarily large quantity of alkaline carbonates: according both to his experiments and those of Geiger, the lymph contains that strongly basic albuminate of soda which, in the absence of other alkaline salts, communicates no alkaline reaction to the solution, and even when coagulated retains much alkali.

Fat occurs in the lymph only in small quantities, and is for the most part in a saponified form: in the lymph of the horse Nasse found 0·0088% of free fat and 0·0575% of alkaline salts of fatty acids, while in human lymph Marchand and Colberg found 0·264% of a pale reddish coloured fat.

The *extractive matters* of the lymph have not been closely examined, although their quantity in relation to the albumen is by no means small. In horses' lymph Nasse found 0·0755% of extractive matters soluble in alcohol, and 0·9877% soluble in water only, while according to Geiger and Schlossberger, the whole of the extractive matters amount to 0·27%.

Nasse was unable to detect *urea* in the lymph of the horse.

We have already noticed the existence of *lactates* in the lymph. (See vol. i., p. 95.)

As in all the animal fluids *chloride of sodium* is the preponderating mineral constituent; in horses' lymph it amounted, according to Nasse, to 0·4123%.

Moreover, *alkaline carbonates* were found by Nasse in horses' lymph, but Geiger failed in detecting them; Nasse calculates their quantity at 0·056%, and he assured himself of their presence by observing, with the microscope, the development of bubbles of gas on the addition of acetic acid. In the ash of the solid constituents of the lymph, Geiger also found an abundance of alkaline carbonates.

The presence of *ammoniacal salts*, which was suspected by

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* Simon's Beitr. z. phys. u. pathol. Chem. Bd. 1, S. 449.

Nasse, has been definitely established in horses' lymph by Geiger and Schlossberger.

Nasse found that horses' lymph was comparatively rich in *sulphuric acid*, which existed there pre-formed: he calculated the quantity of sulphate of potash at 0·0233%.

Alkaline phosphates occur only in very small quantities in the lymph.

The *earthy salts*, with a little peroxide of iron (arising probably from the presence of a few blood-corpuscles), were found by Nasse to amount to only 0·031% in horses' lymph.

The *quantity of water* in the lymph appears to be very variable, but never to be nearly so great as in the blood-plasma; in human lymph Marchand found 96·926%, and L'Heritier 92·436% of water; in the lymph of horses the quantity has been found to vary from 92·5% (Lassaigne) to 98·37% (Geiger).

Nasse has instituted an interesting comparison (based on direct analyses) between the composition of the lymph and of the blood-serum of the horse, from which it follows that the individual salts stand to one another in precisely the same ratio in both fluids, although their absolute quantity is very different in consequence of the larger amount of water in the lymph. Besides the differences in the amount of water in the two fluids (the water of the blood-serum being 7·8%, and that of the lymph being 5·0%), there are also considerable differences in the proportions in which the mineral constituents stand to the organic matters in the two fluids; while 100 parts of salts correspond to 1036 parts of organic matters in the blood-serum, the ratio in the lymph is as 100 to only 785; according to Marchand and Colberg, human lymph contains inorganic and organic matters in almost equal parts.

It is hopeless at present to attempt to calculate the *quantity* of lymph contained in the whole animal body, since we have no fixed points of support to assist us in such a calculation. Even if the lymph of different parts were not so variously constituted as from certain facts and on theoretical grounds appears to be probably the case,—and if the rapidity of the lymph-current in the different vessels (before and after the passage of the lymph through the glands) were not so various, and, moreover, so dependent on internal and external (that is to say, physical and chemico-physiological) conditions, as has been shown by Noll,*—we should still be far less able to calculate the capacity of the lymphatics

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* Zeitschr. f. rat. Med. Bd. 9, S. 52—93.

than of the blood-vessels, since we are much less acquainted with the anatomy of the former than of the latter. We referred, in our remarks on the quantity of chyle formed in a definite time, to the reasons, which render the amount of fluid escaping from the main branch of a lymphatic system, an inefficient criterion of the quantity of this juice formed within any given period. The following facts may, however, aid us in arriving at an approximate idea of the quantity of lymph formed or flowing into the vessels: Collard de Martigny* found that 9 grains of this fluid flowed in 10 minutes from the thoracic duct of a rabbit which had fasted for 24 hours. J. Müller assumes the capacity of the four lymphatic hearts which he discovered in the frog, at about 4 cubic lines, and as these would make about 60 pulsations in a minute, these four lymphatic hearts would drive about 240 cubic lines of lymph into the veins in this period, provided that they are completely emptied at every contraction, which, however, is not the case. Moreover, the lymphatic system is of far more relative importance in frogs and cold-blooded animals than in those in which there is warm blood.

The *origin* of the lymph has been referred by all physiologists to the juice which flows from the capillaries into the parenchyma of the organs, either for their nutrition or for the formation of the secretions. Although physiologists had previously shown that the character and quantity of the lymph depend upon the fluid conveyed through the capillaries, and transuded from them, these views have recently been fully confirmed by Noll. It therefore now only remains for the chemist to institute an accurate comparison of the blood-plasma, the parenchymatous fluid, the secretions and the lymph, in order to deduce the chemical equations giving the scientific expression for the processes which give rise to the formation of the lymph. We are, however, still very far distant from the attainment of this aim, towards which our chemical investigations ought to be directed; for even if we assume that the differences in the transuding blood-plasma and the resorbed lymph can be investigated with chemical accuracy in the same individuals, we are yet unable to draw any certain conclusions in reference to the metamorphoses which the blood-plasma undergoes in each individual organ, or even generally, or to trace the origin of the separate constituents of the lymph. Moreover the lymph which is accessible to chemical inquiry by means of the physiological aids at present at our command, cannot be regarded as the product of the nutrition of these organs. For there is not only a larger quantity of plasma exuded through the

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* Journ. de Physiol. T. 8, p. 266.

capillaries than is necessary for the nutrition of the organs and the formation of the secretions (so that a large proportion of unchanged plasma is blended with the substances which are either metamorphosed by nutrition, or have not passed into the secretions), but it is further proved by innumerable physiological facts, that the fluid which is resorbed by the lymphatics undergoes further metamorphoses in its passage through the lymphatic glands. It may be inferred from the appearance of cells which, however, are probably not formed until after the passage of the absorbed fluid through the glands (at least in the animals provided with lymphatic glands), that the lymph contains not only the products of regressive metamorphoses, but even true plastic substances. The lymph of certain organs appears to possess so high a degree of plastic force, that blood-corpuscles are even formed in it; the lymph of the spleen frequently, and indeed generally, contains blood-corpuscles, as has been already noticed. According to Huschke,* the Malpighian corpuscles of the spleen are nothing more than dilatations of the lymphatics, but from the coincident observations of Gerlach† and Schaffner,‡ it seems much more probable that this organ is one of the main factories for the blood-corpuscles. If, however, the lymph must vary according to the quantity of unchanged blood-plasma which it may contain, we find a new ground established for the great differences which it presents in different parts, when we consider that the chemical constitution of the transuded plasma depends upon the character of the capillaries of each organ, that is to say, upon their width, upon the density of their walls, the velocity with which the blood streams through them, &c. Gerlach draws especial attention to the fact that the spleen has very wide blood-vessels, which may be classed amongst the capillaries from the absence of a circular fibrous coat, and which would appear from the thinness of their walls to be better adapted than the capillaries of other organs to admit of the transudation of a perfectly unchanged blood-plasma, that is to say, of an intercellular fluid, and would therefore afford the most abundant materials for the formation of cells. If we may regard certain normal or even dropsical exudations in the animal body, as for instance, the transudations of the choroid plexus of the brain (which are very remote from the lymphatics that lie only on the periphery), as the direct secretions or

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* Lehre von den Eingeweiden. S. 175, ff.

† Zeitschr. f. rat. Med. Bd. 7, S. 75—82.

‡ Ibid. p. 345—354.

transudations of the capillaries, the view which is based on the difference in the capillaries will derive additional support from the chemical investigation of the transudations of the different capillary systems. Thus, for instance, C. Schmidt* has drawn the following conclusion from the comparison between the composition of the transudation of the capillaries of the peripheral membranes of the brain, and that of the transudation which issues from the central capillaries of the same organ; namely, that the fluid of the brain and spinal cord is by no means mere blood-plasma separated, as it were, by mechanical filtration from the more widely circulating blood-cells, and robbed of some portion of the nitrogenous and fatty matters, which are taken up by the cerebral substance. When we proceed to consider the exudations, we shall have to revert to those investigations of Schmidt which tend to show that the fluids permeating through the different capillary systems of the body possess a constitution, which, although constant for the same system, differs in the different systems, exhibiting its principal differences in respect to the amount of albumen, while the inorganic constituents remain nearly the same as in the blood. According to Schmidt's investigations, protein-bodies transude through the capillaries of the pleura in the largest quantity; scarcely half so large a quantity passing through the capillary vessels of the peritoneum, still less through those of the brain, and least of all through those of the subcutaneous areolar tissue.

These, and similar points of consideration, appear to us to be necessary for the establishment of a physiologico-chemical investigation of the origin and physiological import of the lymph; for any chemical equation would afford a false representation of the sources of the lymph, and of its importance in respect to animal life, if it were derived from the simple chemical analysis of the lymph of the larger vessels, without reference to these points. Unfortunately, however, we are here merely on the borders of a department in which we scarcely know the course or the direction which may lead us to the object of our inquiries. Nasse was the first who endeavoured to throw light on this subject, by comparing, as we have already mentioned, the serum of the blood of the horse with the lymph taken from the cervical region of the same animal. The following are the results of this inquiry.

The lymph always contains more *water* than the liquor sanguinis; hence it is not perfect plasma which is exuded from the blood; but proportionally more water and less solid constituents

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* Charakteristik der Cholera, u. s. w. S. 124—148.

are transuded, than correspond with the liquor sanguinis. The circulating blood must therefore be more concentrated.

On comparing the solid constituents of the lymph and of the serum, we find that the former contains far less *albumen* than the latter; with every 100 parts of soluble salts there occur in the blood-serum 838, and in the lymph only 697 parts of albumen. This relative deficiency of albumen in the lymph cannot merely depend upon the circumstance that less albumen has originally escaped from the capillaries, but principally on the fact that a portion of it has been applied to the restitution of the textural elements which have become effete, as well as to the formation of the lymph-corpuscles.

Moreover, we find far less *fat* in the solid residue of the lymph than in that of the blood-serum; Nasse found the ratio of the soluble salts to the ether-extract to be 100 : 1·57 in the lymph, and 100 : 4·8 in the serum. Since it follows from the examination of morbid transudations that they contain very little fat, we might assume that the excess of fat remains in the serum, especially since the venous blood has been found to be richer in fat than the arterial; a part, however, of the transuded fat may be applied to the formation of cells within the lymph, although in Nasse's comparative analyses, the fibrin and lymph-corpuscles are calculated with the albumen, and hence their fat is included in the analysis of the residue of the lymph; on the other hand, the neutral fats extractable by ether have become in part saponified, and must be sought for in Nasse's alcohol-extract.

The solid residue of the lymph contains relatively more *extractive matters* than that of the serum; if we here also take 100 parts of soluble salts as the standard of comparison, the ratio (according to Nasse's analyses) is as 100 : 50·4 in the serum, and as 100 : 87·0 in the lymph. This augmentation of the extractive matters in the lymph seems obviously due to the *detritus* of the more or less active metamorphosis of the tissues, although a portion of this *detritus* probably transudes from the capillaries even more readily than the soluble salts; at all events we generally find far more extractive matters in the morbid transudations of the capillaries than in the blood. Hence these matters cannot be regarded merely as the remains of textural metamorphosis, but also of the cell-formation already existing in the blood. There are, however, undoubtedly concealed in the extractive matters a number of substances, whose accurate chemical examination promises to throw much light on the metamorphosis of the animal tissues.

According to Nasse's analyses, there is an augmentation of the alcohol-extract in the lymph; this is due to the soaps that are formed, and to the lactic acid and the urea. It is true that no urea can be directly detected in the lymph, but we can hardly do otherwise than suppose that the urea—a product of the metamorphosis of tissue—passes rapidly through the lymphatics before it reaches the blood and is finally separated by the kidneys. The fact that Schmidt* found urea in the fluid in chronic hydrocephalus, might probably be taken as a proof that urea is necessarily present in the lymph, if the non-existence of a simultaneous renal disease had been demonstrated in this case; and Scherer's admirable discoveries regarding the secreted matters found in the parenchyma of the spleen speak still more strongly in favour of this view. Nasse certainly assumes a regressive movement of the transudation, or of some of its constituents, into the capillaries, and according to this view these secreted matters might also be taken up directly from the parenchymatous fluid by the capillaries, but not by the absorbents; but although, according to the experience of several observers, the lymphatics certainly appear to make a selection in the substances which they absorb, yet the latest investigations of physiologists (and especially those of Noll) regarding the force which propels the lymph, indicate that it is the pressure proceeding from the capillaries which chiefly occasions the movement in the lymphatics. It not to be expected that, under the pressure which the lymphatics tend to lessen, any considerable part of the transudation could be reconveyed into the capillaries by an opposite current.

According to Nasse's analyses, the ratio of the water to the *soluble salts* is as 100 : 0·871 in the blood, and as 100 : 0·561 in the lymph of the horse. Hence, even in the normal state, the quantity of water which transudes from the capillaries is even proportionally greater than that of the soluble salts which escape. No one will, however, believe that the water which is formed by the metamorphosis of the tissues contributes in any essential degree to the augmentation of the water in the lymph. The venous blood is consequently found to be poorer in water than the arterial blood. Unfortunately the ash-analyses of the residues of the lymph and serum which were instituted by Nasse, are not of a nature to warrant our drawing any exact conclusions from them. Future and more accurate analyses must show whether the same relations hold in the lymph that Schmidt found to occur in

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* Op. cit. p. 123.

dropsical transudations; that is to say, whether on the whole the salts remain the same as in the blood, excepting that the chlorides are rather more abundant than the phosphates, and that the salts of soda preponderate over those of potash. We may conclude from the analyses of the lymph made by Nasse and others, that the alkaline sulphates are contained in this fluid in much larger quantity than in the serum of the blood. The only process by which these salts can be produced is the disintegration of the sulphurous tissues with the co-operation of the oxygen escaping with the plasma from the blood.

Lastly, Nasse has found that there are far more earthy phosphates in the serum of the blood than in the lymph; this is, however, only dependent on the circumstance that the albuminates in which the earthy salts are contained, occur in a less proportion in the latter fluid.

From a comparison of these analyses of the blood and of the lymph, it follows that the function of the lymphatics consists not merely in conveying those parts of the tissues which have become effete into the blood, from which, after undergoing further changes they are separated by the organs of excretion, but also in elaborating the still plastic portions of the blood into cells—namely, the blood-corpuscles; for how, if this were not the case, could cells occur directly in the lymph, if it merely carried off the disintegrated remains of the tissues? for what purpose would its motion through the lymphatic glands be suspended, or at all events considerably impeded, if the absorbents were not, like the lacteals, organs for the elaboration and formation of the blood?

TRANSUDATIONS.

While pathologists include under the term *exudations* all kinds of fluid, semi-solid, or solid substances which, in consequence of morbid action have been deposited in serous cavities, or in the parenchyma of organs, and have there undergone many metamorphoses, chiefly in a morphological point of view, we regard it as most expedient, in so far as the interests of physiology are concerned, to draw a distinction between the *transudations* which consist of fluid constituents of the intercellular portion of the blood escaping from the capillaries, and exudations in which a change has already commenced. These transudations include all those fluids which are normally or abnormally effused from the blood-vessels (without laceration) into the parenchyma of organs, or into enclosed or open cavities, or even on the surface of the animal body. Hence we include amongst the transudations the normal secretions of the serous membranes, and not merely those of the lining membrane of the cerebral ventricles, of the pericardium, the pleura, and the peritoneum, but also the tears, the aqueous humor of the eye and the liquor amnii, and especially the parenchymatous fluid or juice which moistens and nourishes the tissues; if these transudations are excessive, they form the albuminous and fibrinous exudations of pathologists. Although pathological transudations are now frequently submitted to chemical investigation, and have been more accurately analysed than the normal transudations, in consequence of the greater quantity in which they accumulate, we regard it as most expedient to follow the purely physiological view regarding the escape of these fluids from the capillaries, lest we should lose ourselves in the labyrinths of pathological systems and pathological fictions; for the assumption of watery and serous transudations, of croupous and fibrinous, and again, of serous and albuminous, can find no support either in physical or chemical physiology. We have already seen, when treating of the lymph (a subject closely allied, in more points than one, to that we are now discussing), that in accordance with the views of the most eminent physiologists of the present day, we must consider the escape of water and certain constituents of the liquor sanguinis through the walls of the capillaries as the result of a physical necessity consequent on the penetrability of the walls of the capillaries, the rapidity of the motion of the blood in them, and the physical and chemical characters of the circulating fluid itself. This variety in the conditions affords at the same time an explanation of the differences in the physical and chemical properties of normal as well as of excessive transudations, and of the uncertainty of those attempts at classifying them, which are based either on their incidental properties, or on the form of the metamorphoses which they are more or less inclined to undergo. Hence, without attempting any system of classification, we will proceed to notice their ordinary physical characters, and their essential and incidental constituents.

The normal as well as the excessive transudations have in general the same *properties* as the intercellular fluid or the serum of the blood; they are colourless, transparent, of a sickly and faintly saline taste, of an alkaline reaction, and generally of lower specific gravity than the serum of the corresponding blood. Their *morphological elements* vary with the surfaces on which they are effused; and hence we may meet with epithelial structures, molecular granules, bodies resembling nuclei and cell-formations, which, however, are not peculiar to transudations; blood-corpuscles only occur in them when the capillaries have become lacerated in consequence of some disturbing influence, and blood has thus been actually mixed with the transudation.

Moreover, the chemical constituents of the transudations are precisely similar to those of the blood-plasma; except that, as has been already noticed in regard to the lymph, all the constituents occur in a less ratio than in the plasma, and hence their water is increased; and further, that some even of the organic constituents are so subordinate, that they appear to be altogether wanting, and under the specially existing conditions, to be incapable of transudation. Hence we might classify the transudations according to the absence of one or other constituent of the plasma, if only we could draw any definite limit, and could exhibit the perfect absence of the substance in question even in special cases.

The absence or presence of *fibrin* in the transudations has in this way occasioned the division of those effusions in the animal body which do not contain blood-cells into two principal classes, namely, into albuminous and fibrinous; or, if they are very excessive, into serous and fibrinous dropsy (Jul. Vogel).* No fibrin is to be found in the normal transudations of serous membranes, and in those excessive effusions which are not accompanied by that affection of the capillaries which we assume to exist in inflammations; it is, therefore, absent in the cases of excessive accumulation of serum which arises either from a disturbed state of the functions of the lymphatics, or from an excess of water in the blood. If, however, the blood-current be much impeded, or if it be perfectly stopped in the capillaries, fibrin always escapes through the attenuated walls of the vessels, and gives rise to more or less plastic exudations. Whether, as Vogel assumes, the transudation in non-fibrinous dropsy proceeds chiefly from the smaller veins, and in fibrinous dropsy from the true capillaries, is a point which must be established by further histological investigations. Some capillaries may, in their perfectly normal state, possess the property of allowing the passage of a fibrinous transudation. If the parenchymatous juice which has become effused for the nutrition

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* Path. Anat. Th. 1, S. 12—35 [or English translation, pp. 33—57.]

of the organs cannot be readily isolated, and if we, consequently, are unable to prove by a direct method that it contains fibrin, yet, independently of the general belief, it is in the highest degree probable that this nutrient fluid actually contains fibrin; for this view is supported by the amount of fibrin occurring in lymph, by the constitution of the nutrient fluid in the lower animals which do not possess distinct blood-canals, and by the constant presence of fibrin in the ordinary plastic exudations, as is very well seen in the non-sanguineous secretion of fresh incised wounds—a secretion which has been accurately analysed by Schmidt.*

Fibrin may very often be contained in the transudations, when, from its small quantity, or from the metamorphoses which it has already undergone, it may evade chemical detection. If we consider that in the plasma of normal blood the quantity of fibrin is only one-fortieth of that of the albumen, and if we suppose that the diminution of the fibrin in the transudation only corresponds to that of the albumen, there could never be more than a very small, often almost inappreciable, quantity of fibrin in the effused fluid; if we further consider that the fibrin in the parenchymatous juices is very often applied to the renovation or reparation of tissues, and that in morbid transudations it soon commences to form the groundwork of morphological structures, we need not wonder that the fibrin is so often found to be absent. Most, however, of the dropsical transudations which depend on too aqueous a condition of the blood, or on a disturbance in the function of the lymphatics, appear to be formed without any simultaneous separation of fibrin; at all events, the fact that too aqueous blood is usually found to be a little richer in fibrin than normal blood, seems to favour the view that in this case the fibrin is retained in the circulating fluid. But however this may be, the fact elicited by Vogel remains established, that fibrinous transudations are far more frequent than is usually supposed to be the case, trusting to ocular examination alone.

The physical and chemical properties of the fibrin occurring in transudations perfectly coincide in all essential points with those of the blood-fibrin; the peculiarities which the transudation-fibrin presents, are solely based on the physical and chemical relations under which it is separated, as in the case of the fibrin of the lymph and chyle, to which reference has already been made: the chemist can lay down no such differences as "a fibrin infiltrated with serum," a croupous or aphthous fibrin, or a pseudofibrin.

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* Charakteristik d. Cholera, S. 134.

The fibrin occurring in transudations most frequently coagulates in the form of those soft gelatinous masses which appear infiltrated with serum, or to which we apply the name of pseudofibrin. We know (see p. 199) that this form of coagulation is entirely dependent on an excess of water in the fluid in which the fibrin was previously suspended; and hence we should wonder why this form of coagulation is not far more frequently found in the dead body than is actually the case, if we did not know that the fibrin is usually extremely slow in coagulating in the fluid which transudes in the living body, and that in consequence of the continuous motion in the cavities of the pleura, the pericardium, and the peritoneum, a flocculent coagulum somewhat resembling whipped fibrin must be formed. Moreover, if we take a chemical view of the subject, we cannot accept the idea of a peculiar morbid fibrin; the peculiar forms in which fibrin coagulates in certain morbid processes, and which have led to this assumption, are entirely dependent on the conditions under which the coagulation of the fibrin takes place. However accurately we observe the different forms of fibrin in the varieties of morbid exudations, and however important may be the observations regarding the capacity for organization or the disintegration of one or other form of coagulation, that part of the exudation which is actual fibrin is not to be distinguished in a chemical point of view from the fibrin of the blood. Neither in croupous nor aphthous, nor in any other fibrinous exudation, have I even once found a fibrin which in its microscopico-chemical or purely chemical examination has proved to be essentially different from the ordinary fibrin of the chemists; amongst other things it may be mentioned, that the one fibrin, like the other, was dissolved after a longer or shorter digestion in a solution of nitre, into an albuminous coagulable substance; there was merely a difference of the time in which the change was completely accomplished; and the time was generally almost in a direct proportion to the coherence of the coagulated fibrin. (The exudation-fibrin was, of course, not digested in a solution of nitre until the mechanically comminuted and washed exudation-coagulum no longer contained a trace of any substance coagulable by boiling or by acetic acid.) In many transudations, especially those in serous membranes (in the fibrinous dropsies of Vogel), the fibrin is held in solution, and does not coagulate till the fluid discharged by paracentesis has been for some time exposed to the action of the air; more than an hour often passes before coagulation takes place; and sometimes we may observe the formation of a coagulum in these fluids after they have stood from 10 to 24 hours (Schwann and Magnus,* Delaharpe,† Scherer,‡ Quevenne§). Moreover, this fibrin does not differ chemically from blood-fibrin; we know also that a "fibrin of slow coagulation" may occur in the blood, of which Polli ‖ has given numerous examples. We certainly cannot always state with accuracy in individual cases what it is that impedes the coagulation, but the causes are generally much the same, namely, moderate attenuation with water, an excess of alkaline salts, abundance of carbonic acid, &c,, which, as we have already seen in p. 196, more or less impede the separation of the fibrin. Moreover, the chemical reactions presented by this fibrin are precisely the same as those of ordinary fibrin.

If we should suppose that the question, whether or not the fibrin in these pathological effusions is of a different kind, could be decided by elementary analyses, we should be very far from the truth; for, as in all experiments of this nature, we should find differences enough, but they would depend upon the impossibility of our obtaining such substances as fibrin in a state of chemical purity, and fit for an elementary analysis; we need not here repeat what has been already stated (in vol. i., p. 352) respecting the unfitness of fibrin for ultimate analysis, and (in vol. i., pp. 29-31) regarding the general cautions requisite in such cases.

With regard to the quantity of fibrin which we find in transudations, it is obvious, from what has been already stated, that it presents very great differences, although it is always somewhat less than that of the corresponding blood-plasma. This obviously only holds good with regard to fresh transudations; for when they have existed for some time in the living body, they may on the one hand be found to have been deprived of a great part of their water, or the fibrinous coagulum may have already passed into a state of cell-formation—an object to which other substances in the transudation, besides the fibrin, may be applied; in these cases we certainly meet with far more fibrin in the transudation than in the liquor sanguinis, if we calculate as fibrin all undissolved or insoluble matters.

No fibrin can be detected in those normal transudations which

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* Müller's Arch. 1838, S. 95.

† Arch. gén. de Méd. Juin, 1842.

‡ Untersuch. z. Pathol. S. 106 u. 110.

§ Journ. de Pharm. Nov. 1837.

‖ Eckstein's Handbibl. des Ausl. Heft. 4, S. 25—32.

accumulate in some quantity in the animal body; as for instance in the moisture of serous sacs, the aqueous humor of the eye, the tears, the liquor amnii, certain dropsical effusions, hydatids, cutaneous vesicles (whether artificially excited or consequent on a skin-disease), or in secretions from the intestinal capillaries, as in the diarrhœa arising from catarrh or drastic purgatives, or accompanying cholera.

Those morbid secretions which are consequent on an acute inflammatory process, and are accompanied by laceration of the capillaries and ulceration, have no claim to be reckoned amongst the transudations, seeing that they are not the products of a simple transudation; these are often very rich in fibrin, but in regard to their general constitution and certain of their constituents, they essentially differ from the simple transudations.

Like the fibrin, the *albumen* occurring in transudations is the same as we find in the blood and in other places; the differences which it exhibits in regard to the character and form of its coagulation are entirely dependent on the relations to which we have often alluded, and which are fully discussed in vol. i., pp. 332-334. Thus, in many physiological and pathological transudations, we find that casein-like albumen, which does not coagulate on heating, is precipitated by dilute acetic acid, and separates in the form of a superficial colourless membrane when its solution is evaporated; we need hardly repeat that this body is albuminate of soda, and possesses none of the essential characters of casein. Although casein has been often asserted to be a constituent of such transudations, and has even recently been declared (by Panum*) to be a normal constituent of the blood, I have never succeeded in finding any substance of this nature in such fluids excepting albumen rich in alkali.

In the normal transudations, as for instance in the liquor pericardii, in the fluids of the cerebral and spinal membranes, the liquor amnii, and all those fluids which contain only little albumen, we can always, with a careful examination, detect albuminate of soda; and the same remark applies to the fluid contained in the bullæ of pemphigus, and to the intestinal dejections in cholera. On the other hand, we occasionally, although rarely, meet with transudations from which all the albumen is precipitated on heating, in the form of small flakes; and those are still more rare which become very turbid on the addition of water, and gradually deposit a sediment of pure albumen; almost all albuminous

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* Arch. f. pathol. Anat. Bd. 3, S. 251—264.

transudations become, however, slightly turbid when very much diluted with water. Scherer* has especially directed attention to transudations of this kind; they are generally such as were not submitted to analysis till long after their separation, or such as are found in certain morbid processes, in which the alkali of the blood is diminished or has been saturated by the occurrence of an acid. It follows from these experiments of Scherer's, that the mere chemical analysis of transudations is in itself of little scientific value; and if we would draw any conclusion regarding the pathologico-chemical process from such an analysis, it is imperatively necessary that we should simultaneously institute a comparative analysis of the blood of the patient from whom the transudation was obtained. This is, moreover, one of the reasons why so very few of the analyses of morbid products at present in our possession can be applied to any scientific purpose.

The quantity of albumen in different transudations is extraordinarily variable; in some transudations, the amount is so small that some observers have believed it to be entirely absent, as, for instance, in the tears, in the aqueous humor of the eye, in the liquor amnii (in the last stage of pregnancy), in the fluid in the lateral ventricles and the spinal canal (in the normal and in the dropsical state), and in the fluid of the cellular tissue in œdema of the extremities. If, however, albumen is never entirely absent in these fluids, its amount in other freshly transuded fluids never reaches that contained in the serum of the blood. It now becomes a question, whether there are any conditions inducing a more copious or a diminished transudation of albumen through the walls of the capillaries, so that certain general rules, if not laws, can be established, in accordance with which there may be an augmentation or a diminution of the albumen in the transudation.

The following is one of these rules:—*The quantity of albumen contained in a transudation is dependent on the system of capillaries, through which the transudation occurs.* We are indebted to the admirable investigations of C. Schmidt† for our knowledge of this rule, which is equally important in the elucidation of the mechanical metamorphosis of matter, and in the explanation of morbid processes; and at which he arrived by a series of carefully conducted parallel analyses of normal and abnormal transudations. Schmidt assumes, that the transudation from every group of capillaries contains a definite and constant

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* Pathol. Untersuchungen. S. 78.

† Charakteristik der Cholera. S. 145.

quantity of albumen. He found the transudation in the pleura to be richest in albumen (= 2·85%); that in the peritoneum considerably poorer (= 1·13%); that within the cranial membranes yet more deficient in this constituent (0·6, or at most 0·8%); and that of the subcutaneous cellular tissue the poorest (= 0·36%). Schmidt found this proportion of the albumen to the effused fluid in the transudations of one and the same individual, who was suffering from Bright's disease; and he convinced himself by further investigations regarding the normal transudation of the cerebral capillaries and hydrocephalic effusions, that not only does the quantity of albumen always remain tolerably equal when there is an excess of the transudation, but also when, after the removal of older effusion, a new transudation occurs through the same capillaries. In the normal cerebro-spinal fluid of a dog, Schmidt found 0·24% of organic matter; in chronic hydrocephalus of a child, at the first and at a second paracentesis, 0·156% and 0·179%, and in acute hydrocephalus 0·37%, 0·649%, and 1·040%; in a pleuritic transudation, obtained by paracentesis, 2·61%; in that obtained after death from the same person, 2·85%; in the first peritoneal transudation, obtained by paracentesis, 0·365%; in the second, from the same person, 0·395%. I collected 33·8 grammes of transudation from the pericardium of a perfectly healthy criminal within three minutes after his decapitation; it contained 0·879% of albumen, with 0·093% of other organic matter, and 0·089% of salts. In the fluid, in a case of hydropericardium ex vacuo (in pulmonary tuberculosis), I found 1·543% of albumen. In examining the dropsical transudations in the dead body of a drunkard with true and well-developed granular liver, I found, in the fluid of the pericardium, 1·063% of albumen; in that of the pleura, 1·852%; in that of the peritoneum, 1·044%; and in that of the cerebral ventricles, 0·564%. In a peritoneal transudation, in a case of cancer of the liver (where the liver extended two inches below the navel), I once found 4·351% of albumen, besides 0·598% of extractive matters, and 0·890% of salts; while, on the other hand, in hydræmia (consequent on chronic ulceration of the follicles of the large intestine), I have found only 1·127% of albumen, with 0·448% of extractive matters, and 1·014% of salts. In the transudation from the cerebral capillaries, in hydrocephalus ex vacuo (cerebral atrophy in an old man), I found 0·144%; in congenital hydrocephalus, 0·012%; and in hydrocele, 6·283%, 4·982%, 4·055%, and 3·410% of pure albumen.

Without quoting any additional results obtained either by myself or under my superintendence, and some of which support, while others are opposed to the law which Schmidt has attempted to establish, I will merely give a few numbers obtained by other chemists; in an effusion within the cerebral ventricles Berzelius* found 0·166%, Mulder 0·055%, and Tennant 0·303% of albumen; in a transudation within the peritoneum, v. Bibra† found 2·9%, Vogel‡ 3·3% in one case and only 0·09% in another, Dublanc (like v. Bibra) 2·9%, Marchand 0·238%, and Simon§ 0·84% of albumen ;in a case of hydrocele the last-named chemist found 4·83% and v. Bibra 4·8%, and in œdema of the feet Simon found 0·70% of albumen

If we compare the results of different analysts, it might seem at first sight that they are opposed to Schmidt's postulate, that the transudation of each individual group of capillaries has a special and a constant composition; but a closer examination of the relations accompanying these transudations renders it tolerably evident that this proposition is unquestionably established, but that, like all natural laws, it is modified in its results or actions by other valid laws, and that thus its direct recognition is not very obvious. We can, therefore, only demonstrate this proposition when we compare with one another the simultaneous transudations of different capillary groups *under identical conditions.* We then certainly find that the relative quantity of albumen is tolerably equal in the different transudations, but we must not hence conclude, as Schmidt seems inclined to assume, that the quantity of albumen in the transudation of each group of capillaries is, under all conditions, represented by a definite number; for different conditions may come into play, which exert an influence on the composition of the transudation. The transudation is not the result of merely a single factor; it depends not only on the thickness or the delicacy of the capillaries, but on the rapidity of the current of blood, and on the constitution of the blood itself. Even if there were not sufficient positive facts to establish the position that the composition of the transudation from the same capillary system varies under different conditions, we might *a priori* conclude that, on the one hand, when the current of blood in the capillaries is very slow, and there is great distension of their walls, the composition of the transudation will be very different from what it would have been under opposite conditions, and that, on the other hand, its composition, and consequently its amount of albumen, will vary

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* Lehrb. d. Ch. Bd. 9, S. 198.

† Chem. Untersuch. verschied. Eiterarten, S. 160 u. 170.

‡ Path. Anat. Th. 1, S. 16 [or English translation, p. 37.]

§ Med. Chem. Bd. 2, S. 582 [or English translation, vol. ii. p. 493.]

extremely with the varying physical and chemical characters of the blood.

The capillaries also appear to vary in their capacity for transudation in different stages of the development of serous membranes; thus, for instance, according to Vogt and Scherer,* the liquor amnii in the human subject contains more albumen and more solid constituents generally during the early than in the last stages of pregnancy. Vogt found 1·077% of albumen in the fourth month, and 0·667% after the sixth month; Scherer found 0·767% in the fifth month, and only 0·082% after the beginning of the ninth month; Mack found 0·370 and 0·264% in the liquor amnii at the full time. Three analyses of the liquor amnii, which were conducted by myself, coincide most nearly with those of Mack.

From the simple application of the few analyses which have hitherto been made, we may, by induction, establish the proposition, that the transudation *will be richer in albumen in proportion to the slowness with which the blood passes through the capillaries.* When the circulation is obstructed in the abdominal veins by the presence of large tumours, we find that the transudations contain a larger amount of albumen than in those cases in which the circulation of the blood in the veins is retarded by lesser mechanical obstructions, such as hepatic disturbances accompanied with contraction of the parenchyma of the liver, &c. When the disturbance in the circulation of the blood in one capillary system is so considerable, as is the case in inflammatory hyperæmia, the transudation will be far richer in albumen; and hence we find that all the fibrinous transudations are on an average far richer in albumen than the so-called serous ones. In the fluid of acute hydrocephalus we find, that while there is an absence of fibrin, there is less albumen than in many other serous transudations, but always a larger quantity than in chronic hydrocephalus, &c.

The constitution of the blood forms a third condition, which exerts an influence on the quantity of albumen, as well as on the general composition of the transudations; for *the poorer the blood is in albumen, the less of this substance will be present in the transudation.* C. Schmidt has, however, decisively shown, with reference to the dropsical accumulations in Bright's disease, where the blood is constantly rendered poor in albumen from the quantity of this substance carried off by the urine, that this diminution, when compared with the transudations in dropsy, arises from other causes. In the transudation dependent on the mechanical obstruc-

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* Zeitschr. f. wissenschaftl. Zoologie. Bd. 1, S. 88—92.

tion of the blood in the abdominal vessels, the blood at the same time being highly albuminous, we find more albumen (as in hepatic affections, heart-diseases, &c.) than in that variety which originates in hydræmic blood (as in Bright's disease, cancer, pulmonary tuberculosis, or after copious losses of the juices, &c.)

In considering the transudations, we must not overlook a circumstance to which we have elsewhere drawn attention, namely, that when the transudations stagnate for a prolonged period in a serous cavity, without being either resorbed or artificially removed, as is most frequently the case in hydrocele, ovarian dropsy, and other dropsical fluids contained in closed cavities, the aqueous and some portion of the saline parts are in general again absorbed, so that the fluid, on examination, appears to be far more concentrated, and richer in albumen, than is in general the case with such transudations.

Even if we cannot anticipate that these propositions can be fully established in science until they have been confirmed by further and more systematically conducted investigations, they yet promise to throw some light on this obscure department of pathological chemistry, and to aid in associating into one distinct scientific whole those disjointed facts which have been concealed amidst a mass of imaginary crases and other chimeras of the same nature. Perhaps we may not be too sanguine, if we look forward to a period in the history of pathology, when these three factors shall yield results from which we may establish a numerical equation which shall express the pathologico-physical process of the transudation.

Although the chemical investigations of the transudations afford us some prospect of a nearer recognition of the mechanical interchange of matter in the healthy and the diseased animal body, they leave us wholly in the dark as to the chemical metamorphoses which these substances undergo during and after their transudation. This is especially the case in reference to those substances which are concealed amongst the *extractive matters;* as for instance, the protein-oxides, pyin, and other matters which probably belong to regressive metamorphosis. These extractive matters consist to a great extent of a substance which is soluble in water, but insoluble in alcohol, and which may be precipitated by basic acetate of lead. It resembles Mulder's tritoxide of protein, but exhibits a different composition when it is present in sufficient quantity to be submitted to an elementary analysis. The same is the case with the substance which is precipitable by acetic acid, and very frequently occurs in the older transudations. It seldom possesses the property, ascribed by Güterbock to pyin, of being soluble in acetic acid, but when we succeed in separating it from the albumen which is simultaneously precipitated by the acetic acid, and otherwise purifying it, it exhibits such a different composition, that we cannot even decide from the analysis whether or not it is a product of the oxidation of protein. This substance does not occur in fresh transudations.

The extractive matters are generally present in larger quantities in the transudations than in the corresponding intercellular fluid or serum of the blood. They are commonly more numerous in the older stagnating fluids than in those which have been more recently separated, and are relatively less considerable in the fibrinous than the serous transudations; whilst in the serum of the normal blood the ratio of the albumen (without fat) to the extractive matters is as 100 to 5, it is as 100 to 8 or even to 16 in fresh fibrinous transudations, and in fresh serous transudations it is as 100 to 12 or even to 30, and in the older serous ones, as 100 to 42, or even to 86. From hence we might conclude that these substances transude from the blood into the cavities in larger quantities than the albumen, and this is proved to be the case by the analyses of normal transudations, as for instance, of the fluid within the pericardium, the cerebral and spinal fluids, the liquor amnii, the tears, and the aqueous humor, in which the ratio rises to 100 : 300; indeed the quantity of albumen may be so much diminished as scarcely to be quantitatively determinable, although its presence may be qualitatively proved by the ordinary tests for the albuminates, as for instance, by Millon's (see vol. i., p. 327). In general, however, the extractive matters present great variations in quantity, partly because they are somewhat increased by the chemical treatment employed for the albuminates, and partly because they stand in very various relations to the quantity of water transuded, either owing to the constitution of the blood, or to the peculiar structure of different systems of capillaries. Then, too, it must be borne in mind, that in the older originally fibrinous transudations, in which morphological formations have been developed, one portion of the albumen passes into these, whilst another part is converted into extractive substances, which may therefore be both relatively and absolutely augmented in the analysis. Hence it would be superfluous to give the various quantities of extractive matters assigned by our analyses to these transudations.

Scherer found in a dropsical ovarian fluid a "modification of *mucin,*" precipitable by water and acetic acid. I have three times observed a similar body in the fluids of hydrocele.

Mack found 0·99% and 0·91% of extractive matters in the *liquor amnii* at the full term of pregnancy, Scherer only 0·06% at the same period, but 0·724% in that of a fœtus in the fifth month.

We find only small quantities of neutral saponifiable and saponified *fats* in the transudations; but even here the nature of the capillaries through which these transudations pass is not without some influence, for the fluids of the capillaries of the cerebral membranes, of the pericardium, of the subcutaneous areolar tissue, as well as of the aqueous humor, are very poor in these substances; although here also, in certain pathological cases, they are often increased relatively to the albumen; but this is only the case when the fluid in question is very deficient in albumen. In transudations which are richer in albumen, the relation between the saponifiable and saponified fats differs little from that exhibited in the blood. We find, however, from a more exact comparison of the individual analyses, that the capillaries must possess a greater permeability for these fats than for the albumen. Thus, for instance, the amount of fat in the solid residue of fibrinous transudations is always somewhat greater than that in the solid residue of the intercellular fluid of the blood; and this probably contributes in some degree to the plasticity of the transudations, to the formation of pus-corpuscles, &c. The liquor amnii forms an exception to the general experience on this point; for in the latter months of pregnancy, when its albumen is diminished, it becomes very rich in fat, and indeed has been found to be actually turbid from the presence of fat-globules: this fat is, however, not a product of secretion of the amnion, but is secreted by the sebaceous glands of the fœtus; in fact it is a portion of the vernix caseosa. Mack* found 0·125 and 0·013% of fat in the liquor amnii, and I found 0·098% at the full period.

The non-saponifiable fats or *lipoids,* cholesterin and serolin, usually occur in transudations in far larger quantity than the true fats: *cholesterin* is especially found in the fluid of ovarian dropsies, and even oftener in the fluid of hydrocele, in such quantity that these transudations present the appearance of opaque fluids in which glistening nacreous bands of crystals may be seen on agitation, or even occur as a soft semi-fluid mass of cholesterin. As a general rule, transudations, and especially those of a normal character, are by no means so rich in cholesterin as to admit of

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* Heller's Arch. Bd. 2, S. 218—224.

a quantitative determination of this constituent; but from the microscopic examination of the ether-extract even of normal transudations, we may arrive at the certain conclusion that the amount of cholesterin in the fluid either exceeds, or at all events very nearly reaches that of the true fats. The capillaries generally have the power under certain, not yet accurately determined, conditions of allowing the transudation of cholesterin in larger quantity than other substances; for it is not only in the above mentioned cases of dropsy that we find accumulations of cholesterin; the choroid plexus of the brain, which secretes a fluid that is very poor in fibrin, is not unfrequently found to be covered with an entire crust of minute plates of this lipoid; and how many analyses are there of the transudations into the peritoneum and pleura, in which the quantity of cholesterin has been noted as strikingly great! Indeed we might almost believe that the walls of the vessels possess a peculiar attractive power for the cholesterin, when we reflect on the atheromatous process which is so common in the arteries, if these accumulations of cholesterin cannot be more simply (even if not completely) explained by the circumstance that water, albuminous substances, and salts, are more readily absorbed from the transuded fluid by the lymphatics, or some other means, than the cholesterin, or that by a process of partial absorption its solvent is taken up and removed, and that it is thus compelled to separate in a solid crystalline form in the cavity in which the transudation occurred.

In a hydrocele-fluid, which formed a tolerably consistent pulp, I found 3·041% of pure cholesterin (amounting to 38·202% of the solid residue), and in another fluid of the same nature 1·569%; Simon,* in a similar case, found 0·84% of cholesterin, with a little olein and margarin.

Serolin, which forms hexagonal or rhombic tablets, whose crystallometric determination has been given in the first volume, and which may be so readily distinguished from cholesterin and crystallisable fatty acids by its peculiar shape, always occurs with the cholesterin in the transudations, but seldom in any considerable quantity.

Since Pettenkofer's discovery of his admirable test for the detection of the *resinous acids of the bile*, many chemists who have investigated morbid transudations have met with these substances in dropsical fluids; and it was only to be expected that these substances, if they occurred in the blood, should also simul-

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* Medic. Chem. Bd. 2, S. 582 [or English translation, vol. 2, p. 495.]

taneously pass into the transudations. In every case in which I have hitherto examined dropsical effusions dependent on affections of the liver, I have found in the alcoholic extract, if it has been previously extracted with ether, and usually also in the ether-extract, substances which gave the well known reaction very distinctly and rapidly, so that they could not be confounded with olein. In dropsy from heart-disease (without any secondary affection of the liver) or from Bright's disease, I never succeeded in detecting these biliary matters. On the other hand, I was much surprised to find unquestionable traces of the resinous biliary acids, together with large quantities of cholesterin, in two cases of hydrocele, when neither by physical examination of the patients, nor from the history of their cases, could I detect any evidence of an existing or previous hepatic affection. This circumstance must remain unexplained till further investigations are instituted.

I must not altogether omit to mention, that from the alcoholic extract of the liquor amnii, and still more from that of the vernix caseosa of an infant that had gone its full time, I obtained a substance which, although precipitable only by basic acetate of lead, gave no biliary reaction with sugar and sulphuric acid: the ammonia-salt of this acid crystallized under the microscope in broad plates.

That *bile-pigment* passes into the transudations, both normal and morbid, in cases of icterus, was long ago inferred from the characteristic colour of such fluids, and has subsequently been placed beyond a doubt by chemical experiments. It is, however, remarkable that in the two above mentioned cases of hydrocele, in which resinous biliary acids were found, traces of bile-pigment were also present, besides a very large amount of cholesterin. Its presence might have been very easily established with certainty, but it was not rendered perceptible until a part of the albumen had been precipitated from the fluid by acetic acid, when, on boiling, there was formed a green coagulum, and the supernatant fluid appeared of a somewhat deep green colour.

Heller has arrived at similar results in his investigation of various putrid, purulent, sanguineous hydrocele-fluids; but he also found uric acid, urea, margarate of soda, and glycocholate of soda in abundance.

It has been already mentioned (in vol. i., p. 291) that *sugar* is found in the serous exudations in diabetes, in the same manner as bile-pigment in icterus. After the discovery of this substance in healthy blood, it might be expected that it would likewise occur in the ordinary transudations, but there is no direct proof that this is the case, since the quantities which we obtain for analysis are generally too small to allow of an accurate search for sugar.

In a kilogramme and a half [or nearly three pints and a half] of the peritoneal transudation of a drunkard with granular liver (a quantity which would have been quite sufficient for the determination of sugar, if it had been present in the same proportion as in normal blood-serum), I sought in vain for this substance; but after what has been already remarked (see p. 90) regarding the formation of sugar in the liver, it is probable that the production of sugar is interfered with in cases of hepatic disease, which might account for its not being found in this case.

We have already spoken (in vol. i., p. 166) of the occurrence of *urea* in normal and excessive transudations. Since this substance has been found even in the aqueous humor as well as in the liquor amnii, and has also been detected by C. Schmidt* in the fluid exudation in a case of chronic hydrocephalus in which no renal disease was present, we might fairly assume that it occurs in the circulating blood, and escapes through the walls of the capillaries in these parts with the water and other substances which permeate easily, and is then found in the exudations in a quantity corresponding to the amount of urea in the blood; indeed, if the functions of the lymphatics were disturbed, it might even accumulate in larger quantity, since in all probability it passes through the animal membranes far more readily than other organic substances, or at all events as easily as the alkaline salts. Hence the reason why it is so frequently met with in the transudations in renal affections is simply this, that under these circumstances it accumulates in the blood in much larger quantities than usual, and such as admit of being easily detected.

Marchand† once found 0·42$\frac{0}{0}$ of urea in a peritoneal effusion in a woman, which contained 4·78$\frac{0}{0}$ of solid constituents.

Since urea is often found in such large quantities in the exudations from the capillaries, we should naturally expect that the other products of retrograde metamorphosis (whether as yet detected or not in the blood), as for instance, hippuric acid, creatine, uric acid, &c., would also occur there; but these, and such like substances, have at all events not as yet been recognised in such fluids by any analyst. It is more than probable that creatine

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* Charakteristik der Cholera. S. 124.

† Journ. f. pr. Ch. Bd. 11, S. 458.

occurs in the liquor amnii, for Scherer obtained from it, by means of chloride of zinc, a substance very similar to Pettenkofer's creatine and zinc compound.

In addition to the salts formed by the combination of the alkalies with fatty acids (the soaps), the transudations likewise contain other organic-acid salts; the alkali in them is certainly for the most part in combination with the albumen, but, as has been already mentioned, we sometimes find no albuminate of soda in the transuded fluid, and yet the ash is rich in alkaline carbonates: indeed, every transudation, if it only contains this alkaline albuminate, also contains other compounds of alkalies with organic acids, which dissolve readily in spirit, and impart to the alcoholic extract its well-marked hygroscopic properties. If the spirituous extract has been freed as completely as possible from fat and fatty acids, we yet always obtain carbonates on incineration. But what the acid is, and whether there are more acids than one, are points which cannot be determined in consequence of the small quantity of the substance or substances in question in the transudation, and even in its solid residue. We should be somewhat inclined to believe that this acid in combination with an alkali might be *lactic acid*, since this acid must at all events pass from the muscles into the blood, and must likewise be conveyed to the blood by the process of digestion. Those disturbances of the circulation on which excessive transudations depend, are usually associated with a diminished interchange of gases in the lungs, and consequently a less regular oxidation of the combustible constituents of the blood: hence it is very probable that under such conditions alkaline lactates make their way through the capillaries in excessive quantity, and that the absolute and relative augmentation of the alcoholic extract (as well as of its ash) in the transudation, as compared with the blood-serum, depends on its larger quantity of lactates. If the blood becomes acid, as Scherer* has shown to be the case in many forms of puerperal fever, it is very natural that the transudations should also contain a free acid; in these cases, Scherer has convinced himself, by direct analysis, of the presence of lactic acid. In a transudation of this nature he found 0·105% of free hydrated lactic acid.

We do not meet with true acid transudations, except when the blood previously contains a free acid; for, in the first place, it is improbable that the walls of the capillaries should, during the act of simple transudation, possess the power of decomposing the salts

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* Untersuch. z. Pathologie. S. 147—194.

of the blood into acids and bases, and that they should allow only of the transudation of the former; in the simple *transudations* no supplementary development of free acid appears, however, to occur; it is only when suppuration and similar processes have taken place in *exudations* that the fluid is observed to have an acid reaction; indeed, it is generally dependent on a process of fermentation set up in the fat.

Simon* once examined a specimen of the fluid of pemphigus which had a strong acid reaction; he considered the free acid to be the acetic, in consequence of its apparent volatility; this was doubtless an uncommon condition; the fat, in this case, as in ordinary pus, may undergo butyric fermentation; for all *vesicular cutaneous eruptions*, whether they are produced artificially by vesicants, or are the natural morbid phenomena of pemphigus, herpes, or eczema, have an alkaline reaction, and contain albumen, as Andral† had formerly observed, and belong to the simple transudations. It is only the vesicular cutaneous eruption, which is known as sudamina, which invariably presents an acid reaction; it, however, does not arise, like the other vesicular eruptions, in consequence of local congestion; the fluid within the vesicles in sudamina contains *no albumen*, and hence is not to be classed amongst the transudations. We shall return to the causes of this acid reaction when we treat of the sweat.

Heintz‡ has found a crystallizable organic acid, which sublimed without decomposition, and presented a very great similarity to succinic acid in the fluid of cysts containing echinococci (see vol. i., p. 74); as Dessaigne§ has proved that succinic acid may be formed from butyric acid by oxidation, we need no longer regard the occurrence of succinic acid in the animal organism as extraordinary.

It may be readily inferred from some of the preceding observations that the *soluble mineral salts* transude through the walls of the capillaries in larger quantity than any organic matter; but a review of most of the good analyses of these exudations, in so far as the subject has been yet investigated, leads us to regard the following points as established: water in every case transudes in the greatest quantity; the fibrinous transudations which approximate most nearly to the plasma, in reference to their amount of solid constituents, contain almost constantly *rather less salts than*

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* Med. Chem. Bd. 2, S. 579 [or English translation, vol. 2, p. 488].

† Compt. rend. T. 26, p. 650—657.

‡ Jenaische Ann. d. Physiol. u. Med. Bd. 1, S. 180—191.

§ Compt. rend. T. 30, p. 50.

the intercellular fluid; while the average amount of mineral substances in the latter is about 0·85%, we usually find in fibrinous transudations from 0·73 to 0·82% of salts. In the true dropsical accumulations the proportion of the salts is, however, very different; such fluids contain an amount of salts often exceeding that which is found in normal blood-serum, the number sometimes rising to 0·86, or even to 0·95%; here, however, the general rule also holds good, that the transudation contains rather less salts than the *corresponding* liquor sanguinis; for in dropsy the blood is always rich in salts, as we have already seen in page 252. In proportion to the richness of the dropsical blood, so much the richer in salts is the transudation; the latter, however, always contains a fraction less salts than the former. This proposition can only be established by a careful comparison of all the analyses which we at present possess; but the careful investigations of Schmidt have rendered it certain that it may be regarded as a law which may be expressed by a general formula. Schmidt has, however, further shown that this rule presents an exception when, simultaneously with the transudation in the interior of the body, there is an elimination of albumen externally, that is to say, when albuminuria is at the same time present: in that case, a larger quantity of salts, and far less albumen, transude through the capillaries of the peritoneum into its cavity than would have been the case if there were no external loss of albumen; hence in such cases the number representing the mineral salts often equals, and may even exceed, that of the organic matters.

A similar condition to that which we have just noticed may occur with regard to the amount of salts in the liquor amnii: in the fifth month of pregnancy we find, according to Scherer, 0·925% of salts with 0·767% of albumen; the albumen is here not lost, but is otherwise applied, and hence the considerable and extraordinary augmentation of the salts in the transudation of the amnion: towards the end of pregnancy the ratio of the albumen to the salts is still more unfavourable; in these cases there has been found only 0·37% of albumen with 0·92% of salts, and Scherer found actually only 0·082% of the former with 0·706% of the latter.

The relative proportion of the salts in the transudations through the intestinal capillaries in cholera, or in diarrhœa after drastic purgatives, is altogether peculiar; in these transudations the quantity of the salts is five, or even seven times as great as that of the albumen; at the same time they are richer in water than those of any other kind; there is here no direct proportion between the composition of the blood and that of the transudation, as in the dropsical effusions; but we rather observe that the fluids stand in an inverse relation to one another, the blood being poorer in water, poorer in salts, and far richer in albumen, than the effused fluid. (See our observations on the evacuations and the blood in cholera, pp. 151 and 264.)

The salts occurring in the transudations are precisely similar in their nature to those of the intercellular fluid, and they are found in almost exactly the same relative proportions to one another in the transudation and in the blood-serum; as in the latter fluid, the chlorides considerably preponderate over the phosphates, sulphates, and carbonates, and the soda-compounds over those of potash. A very important exception to this rule, in so far as the physiology of secretion is concerned, has been observed by C. Schmidt in the constitution of the salts which occur in the fluid within the lateral ventricles of the brain (the transudation from the choroid plexus). Whilst the transudation from the pia mater and arachnoid contains the salts in precisely the same proportions as occur in the fluids of other serous membranes, the mineral constituents here contain a great excess of potassium-compounds and phosphates, so that the proportion of the potassium to the sodium, and that of the phosphates to the chlorides, approximates more nearly to that which is presented by the salts contained in the blood-cells. While (according to Schmidt) there are contained in the salts of the transudation from the peripheral cerebral capillaries 2·8% of potassium with 40·0% of sodium (a ratio almost identical with that which is presented by the salts of the serum), the salts of the transudation from the choroid plexus contain on an average 17·8% of potassium, and only 27·2% of sodium. In the same manner the constitution of the transudation within the lateral ventricles approximates to that of the blood-cells in regard to the chlorides and phosphates; while in 100 parts of the salts of the serum there are contained 5·6 of phosphoric acid with 45·2 of chlorine, Schmidt found 8·9% of phosphoric acid and 37·6% of chlorine in the salts in central hydrocephalus. Hence the cerebro-spinal fluid is not to be regarded as a mere *transudation* or filtrate from the blood, but as a peculiar *secretion* in whose formation the blood-corpuscles appear to take an essential part in so far as the salts are concerned.

We may further readily convince ourselves that *alkaline carbonates* are also present in the normal alkaline transudations, by placing fresh fluids of this kind which have been obtained by paracentesis in a vacuum, and as completely as possible removing the gas, then adding acetic acid without allowing the access of air, expelling from the serum the absorbed carbonic acid which has been liberated by the action of the air-pump, as well as by displacement with hydrogen gas, and determining it in the ordinary manner; in short, by applying the method which I* adopted for the determination of the combined carbonic acid in the blood.

In cholera, and after the use of drastic purgatives, the composition of the salts in the transudations—that is to say, in the intestinal dejections—differs essentially from that in ordinary effusions; here, according to the accurate investigations of Schmidt, the compounds of chlorine and sodium preponderate over the phosphates and the potassium-compounds even to a greater extent than in ordinary transudations. On the other hand, transudations of any other nature that may accompany the cholera process generally present the opposite relation to the ordinary serous effusions; whilst, for instance, in other cases, the normal as well as the excessive transudations from the cerebral capillaries contain only a small amount of solid constituents, in which the mineral substances preponderate over the organic in ratios varying from 5 : 2 to 17 : 4 (or from 2·5 : 1 to 4·25 : 1), we find that in cholera the cerebral transudations are not only far richer in solid constituents, but that of these the organic actually exceed those of a mineral nature; amongst the latter the compounds of sodium and chlorine occur, however, in far less quantity than in ordinary transudations; indeed the potassium-compounds and the phosphates must preponderate the more, since the serum in cholera contains far more of these compounds than normal serum. Unfortunately, Schmidt had no opportunity of making an accurate analysis of the salts of the cerebro-spinal fluid in cholera, in order to prove by numerical results the preponderance of the phosphates and of the chloride of potassium in this transudation.

No *salts of ammonia* can be detected in normal and fresh transudations obtained by paracentesis (see vol. i. p. 452); and if some observers have believed that they had found them, this was dependent on the causes of error to which we have already alluded. Even in several secretions of long standing in the tunica vaginalis testis, I was unable to recognise ammonia with certainty. If indeed we attach any importance to the analyses of fluids actually becoming putrid, we might then always find ammonia; and, on the other hand, we must of necessity always find ammonia in the intestinal transudations, since the decomposition of such substances proceeds

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* Berichte d. k. sächs. Gesellsch. d. Wiss. Bd. 1, S. 96—100.

with such extraordinary rapidity in the intestine, that we must altogether abstain from analysing them, if we wait till we can obtain them in their perfectly pure, native state. Ammonia must, however, be found, and indeed has been found by Schmidt in all transudations arising from blood containing ammonia or much urea (see p. 264), and hence it is not uncommonly met with in dropsical exudations in albuminuria.

Finally, we may very readily convince ourselves that the transudations, like the animal fluids generally, contain free *gases*, by employing a simple gas-apparatus in communication with the air-pump. Amongst the mixture of gases that are evolved from the transudation, carbonic acid is found to preponderate, although the presence of oxygen and nitrogen may be recognised with certainty. From determinations which can certainly only be regarded as approximate ones, I obtained from fresh transudations discharged by paracentesis, on an average, a less quantity of gas generally, but always relatively more carbonic acid than from the fresh blood-serum of persons for whom venesection had been prescribed solely in consequence of plethora.

The apparatus which I employed for this somewhat superficial investigation was constructed in the following manner: Two flasks are united to one another by glass tubes and corks; in the lower one we place the fluid to be examined, and in the upper one, which is two-necked, we place pure almond or olive oil; from the lateral tube there proceeds a glass tube filled with oil to the bottom of a third flask; this last flask, whose bottom is covered with oil, is brought in connexion with the air-pump. On now making a vacuum, the bubbles of gas which are developed from the blood rise into the upper flask (which stands reversed upon the lower one), and drive the oil through the communicating tube into the third flask; if now we allow air again to enter the last flask, the oil is only in part forced back into the upper flask; the bulk of the gases contained in it is diminished to the volume corresponding to the external atmospheric pressure. Since any resorption by the aqueous fluid in the lower flask is prevented by the oil, we may at all events form some idea of the quantity of gases which such fluids contain.

It is unnecessary to give a special description of the different methods which may be devised for the qualitative and quantitative analysis of the transudations, since the same rules hold here which we have fully noticed when treating of the "analysis of the blood" and of the individual animal substances, in their respective chapters in the first volume. We may, however, be permitted to make the single remark that here, as indeed in every investigation of an animal fluid, the microscopical analysis must always precede the chemical. Thus, for instance, the presence of blood-corpuscles would at once destroy any claim that the fluid might otherwise possess to the character of a pure transudation; again, if the object itself be not pure, the results of the experiment must be in a corresponding degree worthless. The same observation equally applies if vibriones and other formations which accompany putrefaction are present. If none of these are to be observed, we may frequently perceive cells in the transudation, which resemble lymph-corpuscles or pus-cells. Without further investigation, they have, however, no more claim to be considered as pus-corpuscles, than those which are produced from mucous membranes; it is only when true pus is present (and in some cases it is very difficult to decide this point) that the object should be regarded as not a pure exudation. In transudations which contain no fibrin, the substances in suspension, as for instance fat, epithelial cells, cells in the process of development, and similar bodies, must naturally be separated as far as is possible from the fluid by filtration; if, on the other hand, coagulated fibrin be present, its absolute quantity cannot be determined with accuracy; we must further ascertain by microscopical investigations whether an excess or deficiency of morphological elements be present, and we must obviously take this circumstance into consideration in estimating the quantity of fibrin contained in the transudation.

The *quantitative relations* in which the various transudations, either in the normal or excessive state, are thrown off from the blood, are so various, that no general rule can be established even for each individual capillary system. They become, however, of the highest importance in relation both to the mechanical and the chemical metamorphosis of matter in the healthy and the diseased animal body; but here the amount of the transudation is only of interest in so far as the individual cases have reference to special conditions, and may accordingly be applied to the establishment of a more general view.

As in the preceding pages we have already sufficiently noticed the *genesis* of the transudation, in so far as we need here consider the general metamorphosis of matter, it only further remains for us to allude to the *physiological value* of the normal transudations, and the uses of the abnormal ones as channels for pathological processes (as after inwardly directed crises, &c.); but this is unnecessary, since the former pertains to purely physical physiology, and the latter are altogether beyond the domain of scientific investigation.

MILK.

This glandular secretion, which is peculiar to the mammalia, is generally of a white, but frequently of a bluish-white colour, more rarely of a somewhat yellowish tinge, opaque, without odour, of a slightly sweet taste, and an alkaline reaction. Its specific gravity fluctuates, according to Scherer,* between 1·018 and 1·045, but in women is on an average 1·032 (Simon).

As is well known, milk, when allowed to stand for some time, exhibits on its surface a thick, fatty, yellowish white stratum, the cream, while the fluid below has become poorer in fat, and has, therefore, a greater specific gravity than fresh milk, and has likewise a more bluish white colour. When milk stands in a not very low temperature, it gradually begins to exhibit an acid reaction, remaining for some time thinly fluid, more especially after it has been repeatedly boiled. But if it has not been boiled, and the temperature be somewhat above the mean, and if there should be considerable electrical tension in the atmosphere, the acid will increase to so great a degree that the casein of the milk will be precipitated; that is to say, the milk will coagulate, become thick, and gradually be converted into a moderately thick pulp. The milk may be made to coagulate artificially by rennet, both when it has an acid as well as an alkaline reaction (see vol. i., p. 375). When exposed to rapid evaporation, milk becomes coated with a dense white membrane.

It would, of course, be superfluous to make any remarks as to the *mode of procuring* animal milk; it must, however, be observed, that it frequently is extremely difficult to obtain any considerable quantity of milk from women who are suckling. We need not, however, enumerate any of the well-known manipulations and methods, which are familiar to every practitioner, for procuring a sufficient quantity of milk to serve for a physical examination. The special forms of apparatus employed for this purpose are almost all based upon the principle of rarefaction or suction, but

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* Handwörterb. der Physiol. Bd. 2, S. 449—475.

none appear so perfectly to fulfil their object as the one recently proposed by M. Lampérierre.*

This apparatus is made of caoutchouc, in the form of a mouth, provided with lips, gums, and elastic cheeks, the latter being connected with the short neck of a small tubular retort, into which is introduced a glass tube, which, when necessary, receives the milk, either by the action of the woman herself, or by the aid of a small air-pump.

Fresh milk appears, on *microscopic* examination, as a clear fluid, in which fat-globules, the so-called *milk-globules,* are suspended, as in an emulsion.

These *milk-globules* differ considerably *in size.* The majority have a diameter of from 0·0012‴ to 0·0018‴; and although they are rarely found to measure 0·0038‴ in fresh milk, Henle states that he has found them to be 0·014‴; and, according to Raspail and Donné, they are even sometimes 0·044‴.

When examined under the microscope, without the addition of any chemical reagent, these globules exhibit no trace of any *investing membrane,* although its existence may very readily be demonstrated beyond all doubt, in two different ways. One method, which was suggested by Henle,† consists in observing, under the microscope, the action of diluted acetic acid on the milk. The milk-globules exhibit changes of form under these circumstances which they could not possibly experience if they were mere fat-globules, for they become much distorted, some appearing caudate, and others biscuit-formed. From the greater number there escapes a small drop, which appears almost like the nucleus of a larger globule, and is soon displaced by another small fat-globule, which emerges from the milk-globule, and either combines with the larger globules, or is only made to project in such a manner, that the milk-globule exhibits a faint resemblance to a fermentation-fungus in the process of development. When treated with a less diluted acetic acid, the milk-globules become confluent. Mitscherlich's‡ method, which we described in detail in vol. i., p. 384, proves, in even a more distinct manner, the presence of a membrane round the milk-globules.

Occasionally also the milk exhibits certain morphological elements, which, from their invariable presence in colostrum (the first milk yielded after delivery), have been termed *colostrum-*

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* Compt. rend. T. 30, p. 219.

† Allg. Anat. S. 942.

‡ Göschen's Jahresber. Bd. 2, S. 19.

corpuscles (the *corps granuleux* of French physiologists.) They are irregular conglomerations of very small fat-globules, which are held together by means of an amorphous, somewhat granular substance. Their diameter varies, according to Henle, from 0·0063‴ to 0·0232‴, but may be considered on an average to be about 0·0111‴. The fat-granules of these masses are more easily dissolved by ether than those of the milk-globules; acetic acid and potash dissolve the granular combining substance, and scatter the fat-globules: an aqueous solution of iodine imparts an intense yellow colour to the colostrum-corpuscles. There can, therefore, be no doubt that these molecules are merely very small fat-globules imbedded in an albuminous substance. There is no appearance either of a nucleus or of an investing membrane.

These molecules generally disappear on the third or fourth day after delivery, although they have been found as late as the twentieth day in perfectly healthy women. As a general rule, however, these corpuscles return whenever any disease supervenes after delivery, or in case the mother is attacked by any acute affection.

In all cases in which I examined the milk of women shortly after their confinement or of nurses who were suffering from any acute disease, such as inflammations, acute exanthemata, typhus, &c., I always found colostrum-corpuscles, and, in addition to these, true granular cells, having a microscopically and chemically demonstrable investing membrane, and frequently also an obvious nucleus; the granules of these "inflammatory globules" were tolerably large, transparent, and rich in fat, resembling those which are so commonly observed in the greyish black sputa of chronic catarrh (in the emphysema of old persons).

Epithelial cells and *mucus-corpuscles* are only incidental admixtures of the milk, and are, therefore, more frequently observed in morbid affections than in the normal condition.

Fibrinous coagula only occur when the milk contains blood.

Blood-corpuscles have rarely been found in the milk, and are only present in it in abrasions of the nipples, or in similar affections.

Infusoria, or some of the *lower forms of vegetation*, are occasionally found in cows' milk, especially in the so-called *blue milk*. J. Fuchs* refers this colouring of the milk to the presence of an

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* Handwörterb. d. Physiol. Bd. 2, S. 470.

infusorium, which he terms vibrio cyanogeneus; but Bailleul* ascribes it to a byssus.

My observations on this subject are limited to the ordinary manner in which the milk acquires this blue colour. When freshly drawn, the fluid is generally perfectly white, assuming this peculiar blue shade of colour on the formation of the cream, which exhibits pale blue specks, extending at first scarcely half a line deep, and appearing in detached groups upon the surface of the otherwise white fluid. These specks become darker, and gradually increase downwards and laterally, until they commingle. The curd which separates from the cream is colourless, and the bluish cream contains rod-like, colourless vibriones, similar to those described by Fuchs. I only once observed a distinct formation of byssus.

We have already become acquainted with the most important *chemical constituents* of the milk in our considerations of the organic substrata. This is especially the case with *casein* and *milk-sugar*, which have already been very fully treated of, not only in reference to their chemical properties, but also to their occurrence in variable quantities under different physiological and pathological conditions (see vol. i., pp. 297 and 383). It still remains, however, for us specially to notice the third organic constituent of the milk, namely, the *fat* or *butter*. The fat of women's milk has not yet been subjected to any exact qualitative analysis, but the butter of cows' milk has been carefully analysed by Chevreul,† and more recently by Bromeis‡ and Lerch§. Pure milk-fat is almost colourless, or at most is but faintly yellow; after being melted it solidifies at + 26°·5. It becomes soft and greasy at a temperature exceeding + 18°. One part of this fat dissolves in 28·9 parts of boiling alcohol of 0·822 sp. gr. It easily becomes rancid on exposure to the air, and then forms volatile fatty acids; hence it imparts a somewhat reddish colour to moist litmus paper, even when in a comparatively fresh state. It is perfectly saponifiable, and yields, in addition to glycerine, margaric, oleic, capric, caprylic, caproic, and butyric acids, or in place of the two latter, vaccic acid (see vol. i., pp. 56–71). Bromeis calculated the composition of butter, from the quantity of the acids which he obtained from it, as equal to 68% of margarin, 30% of olein, and 2% of true butter-fat; but this calculation affords only

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* Compt. rend. T. 17, p. 1138.

† Recherches sur les corps gras. Paris, 1822.

‡ Ann. d. Ch. u. Pharm. Bd. 42, S. 46 ff.

§ Ibid. Vol. 49, p. 212.

an approximate representation of the composition of the milk-fat, since its constituents appear to vary considerably under different physiological relations.

The quantity of fat contained in milk appears to vary very considerably, for Simon[*] found in *women's milk* from 2·53 to 3·88% of butter; Clemm[†] and Scherer found on the fourth day after delivery 4·297%, on the ninth day 3·532%, and on the twelfth day 3·345%; Chevallier and Henry[‡] found 3·55%, and Haidlen[§] 3·4 and 1·3%. Simon found in *cows' milk* from 3·80 to 5·10%, Herberger 3·89 and 3·75%, Chevallier and Henry 3·13%, Boussingault[||] 3·90%, Playfair[¶] 4·90% (as the mean of nine observations made on the milk of the same cow), and Poggiale[**] 4·38% (as the mean of ten analyses). Clemm found 6·952% in *mares' milk;* Simon 1·21, and Peligot 1·29% in *asses' milk.* Chevallier and Henry found 4·2% in *sheep's milk.* Fayen[††] found 4·08, Chevallier and Henry 3·32, and Clemm 4·251% in *goats' milk.* Schlossberger[‡‡] found 2·65% in the milk of a buck; and in *bitches' milk* Simon first found 16·2, and afterwards 13·3%; while Dumas[§§] found from 7·32 to 12·40%, and Bensch[||||] 10·75 and 10·95%.

Simon found 5·00% of butter-fat in the *colostrum* of women's milk, and coincides with Boussingault in giving 2·6% as the quantity occurring in that of the cow. Chevallier and Henry found 5·0% in that of the ass, and 5·2% in that of the goat.

L'Heritier found, from a comparative analysis of the milk of two nursing mothers, aged twenty-two years, one of whom was dark and the other fair, that the milk of the former was richer in fat (containing 6·48 and 5·63%) than that of the latter (which contained 3·55 and 4·05%). This observation, which requires to be confirmed by further investigations, is the more remarkable as the other organic constituents were considerably increased in the milk of the *brunette.*

L'Heritier[¶¶] found from 1·62 to 1·70% of casein, and from 7·12

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[*] Die Frauenmilch u. s. w. Berlin, 1838.

[†] Handwörterb. d. Physiol. Bd. 2, S. 464.

[‡] Journ. de Pharm. T. 25, p. 333 et 401.

[§] Ann. d. Ch. u. Pharm. Bd. 45, S. 273.

[||] Ann. de Chim. et de Phys. 3 Sér. T. 8, p. 98.

[¶] Lond., Edin., and Dublin Phil. Mag. Vol. 23, p. 281.

[**] Compt. rend. T. 18, p. 505—507.

[††] Ann. de Chim. et de Phys. 1839, p. 144.

[‡‡] Ann. d. Ch. u. Pharm. Bd. 51, S. 431.

[§§] Compt. rend. T. 21, p. 708—717.

[||||] Ann. d. Ch. u. Pharm. Bd. 61, S. 221—227.

[¶¶] Traité de Chimie pathologique. Paris, 1842, p. 638.

to 7·00% of milk-sugar in the brunette, and 1·00 and ·95% of casein; and from 5·85 to 6·40% of sugar of milk in the blonde.

Peligot made the striking observation, which has recently been confirmed by Reiset,* that the milk which is last yielded during milking or artificial suction, is much richer in fat than that which is first drawn, although the composition of both portions is otherwise the same. It was supposed from these observations, which were at first limited to the ass and the cow, that the milk lost some portion of its cream in the mammary glands, while the more watery and less fatty milk collected in the lower part of the udder; but as Reiset has made the same observations in respect to women's milk, which had been drawn in fractional portions from the breast, the cause can scarcely be dependent upon such simple mechanical relations as these.

Peligot found 6·45% of butter in the first third of the milk of an ass, 6·48% in the second, and 6·50% in the last portion. Reiset found precisely similar relations in the milk of two cows, provided a full period of four hours had intervened between both times of milking; for when the animals were milked after intervals of two hours only, there was no perceptible difference in the various portions of one and the same milking. When the collective milk of a cow yielded 4 5% of fat, the last portions of the milk were found to contain 7·63, 7·53, and 8·40% of butter. The milk of a nurse, aged 27 years (seven months after delivery), yielded more fat after the child had drawn the breast (on an average 5·54%) than before its application (on an average 3·24%).

According to Simon's investigations, the quantity of fat contained in woman's milk remains nearly the same throughout the entire *period of lactation.*

The nature of the food affects, at least in some degree, the quantity of fat contained in the milk. Boussingault† found that cows fed upon carrots, without the leaves of the plant, yielded milk containing 1·25% of fat, while the milk contained only 1·4% of butter when the food consisted of oats and lucerne. Playfair thought he could perceive an increase in the quantity of butter in the milk when the cows were fed on potatoes. The result of experiments made by Boussingault‡ on two cows was as follows: after feeding the animals on beet-root, the milk of one cow was found to contain 4·56%, and that of the other 3·42% of fat; when

* Ann. de Chim. et de Phys. 3 Sér. T. 25, p. 82—85.

† Ibid. T. 11, p. 433.

‡ Ibid. T. 12, p. 153.

the food consisted of the after-crop of grass, the milk yielded 3·92 and 4·39%, and 3·97 and 4·63% when potatoes were used. Payen and Gasparin* found 3·53% of butter in the milk of a cow which had been fed in the ordinary manner, and 4·87% when the food consisted of maize-cake. Dumas found that the milk of bitches was on an average somewhat richer in fat when they had been fed on vegetable than on animal food.

A mere superficial mechanical investigation would be sufficient to show that the milk must be poorer in fat during disease; the fact has, however, been fully confirmed by some exact analyses made by Donné, Herberger, and Simon.

I found 3·39% of fat in a portion of cows' milk, which became blue when the cream had formed. Three weeks after the disappearance of this phenomenon, the milk yielded 4·934% of fat, although the animal was fed on the same food.

No exact investigations have as yet been made on the *extractive matters* found in milk, or in reference to the different quantities in which they occur in different milk.

In reference to the *salts* of the milk, it must be observed, that the soluble salts consist of the chlorides of sodium and potassium, alkaline phosphates, and, in addition to these, of the potash and soda which are combined with the casein in the milk. The insoluble salts consist of the phosphates of lime and magnesia, which principally belong to the casein (see vol. i., p. 379). No sulphates or salts of ammonia are found in fresh milk (see vol. i., p. 444). Haidlen† found a little peroxide of iron in the ash of cows' milk.

The milk of women contains, according to the investigations of most observers, from 0·16 to 0·25% of salts, cows' milk from 0·55 to 0·85%, and the milk of the bitch from 1·2 to 1·5%.

The amount of the *soluble salts* in the milk is in general smaller than that of the insoluble phosphates. There occur about 0·04 or 0·09% of soluble salts in the milk of women, and 0·21% of soluble and 0·28% of insoluble salts in the milk of the cow. According to Dumas, the milk of the bitch contains 0·71% of soluble and 0·77% of insoluble salts when the food has been mixed, and 0·45% of soluble and 0·57% of insoluble salts, when the food consisted of animal substances. Bensch found in the milk of a bitch, which had been exclusively fed on meat, 1·252% of ash, of which 1·165 were phosphates of lime and magnesia.

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* Compt. rend. T. 18, p. 797.

† Ann. d. Ch. u. Pharm. Bd. 54, S. 273.

The ash of cows' milk contains, according to Weber's analysis, conducted by Rose's method, 14·18% of chloride of potassium, 4·74% of chloride of sodium, and 23·46% of potash and 6·96% of soda (combined with phosphoric, sulphuric, and carbonic acids). The ash of ox-blood, on the other hand, after the abstraction of the peroxide of iron, contains 38·82% of chloride of sodium, no chloride of potassium, 29·09% of soda, and only 11·44% of potash. This milk, therefore, independently of the absolutely small quantity of salts, contains a relatively less amount of soda-compounds and alkaline chlorides, but a much larger quantity of potassium-compounds. In the ash of milk we moreover find, according to Weber's analysis, 28·4% of phosphoric acid, while in the ash of the blood (according to the same analysis) there is only 7·74% of this acid, after deducting the iron. Finally, there is 17·34% of lime and 2·20 of magnesia in the ash of the milk, while there is only 1·90% of lime and 0·75% of magnesia in the ash of the blood (after a similar deduction of the peroxide of iron). Hence the milk exhibits a considerable excess of phosphoric acid and earths over the blood. The phosphoric acid present in the milk-ash is almost wholly tribasic. We shall in a future part of the work see the importance of these comparative numbers, in relation to the theory of the secretions and the metamorphosis of matter generally.

Alkaline carbonates are also present to some extent, if not in all kinds of milk, at all events in cows' milk. Thus, when two samples of fresh milk, one unmixed and the other treated with a little acetic acid, be placed under the receiver of an air-pump, and we produce a vacuum, the latter will be found to contain a much larger quantity of gas, that is to say, of carbonic acid, than the former.

Lactic acid is not contained in fresh milk, as we have already shown in vol. i., p. 98, and it only appears to be formed abnormally in the udders of graminivorous animals. The freshly drawn milk of herbivorous animals always exhibits a slight alkaline reaction, and is only rendered acid when the food of the animal has been scanty and poor in quality. It still remains for us to determine whether, in these cases, the acid reaction invariably depends upon lactic acid, or, as may possibly be the case, on the presence of *acid phosphates*, or even on *butyric acid.* The milk of the bitch is, according to Bensch, neutral when the animal has been kept on vegetable food; whilst it is always acid when the food has been exclusively animal. This acid reaction is most probably owing to the acid phosphates, and more especially to superphosphate of lime.

Free *gases*, and more especially carbonic acid, can always be shown to be present in fresh milk, according to the method already described at p. 330.

Abnormal constituents have in general been but rarely found to exist in the milk, although our daily experience of the injurious influence exerted by the milk of some women on the children they suckle, and frequently by that of cows on the life of their calves, clearly indicates the existence of chemical metamorphoses in the milk, and the presence within it of certain abnormal substances. *Albumen* is the most frequent of these abnormal constituents of the milk; it is present in inflammatory affections of the mammary glands, when the milk contains blood and pus; and it is perhaps normally present in the contents of the lactiferous ducts in all periods except during lactation; at all events, Simon found 19·834% of a substance coagulable by heat in the fluid secreted by the udder of an ass, fourteen days before foaling. The colostrum of the cow coagulates on being boiled, but not when treated with rennet. We must not, however, assume that when the milk coagulates on being heated it necessarily contains albumen, for Scherer has obtained a casein from normal milk which coagulated by heat, while both Dumas and Bensch found that the milk of the bitch became pulpy and was even almost completely coagulated on being heated, when the animal had been kept on vegetable food as well as when it was fed on animal matters, while on cooling it very frequently again became thinly fluid.

Marchand[*] found dissolved *hæmatin* in the milk of a diseased cow, without, however, being able to detect any blood-corpuscles under the microscope.

Fibrin occurs in the milk only when the latter contains blood; at least, as far as my own experience extends, it is never present except simultaneously with blood-corpuscles, or at least with hæmatin.

Rees[†] has found *urea* in the milk in Bright's disease.

Much was formerly written regarding the passage of foreign substances, as pigments, medicines, and poisons, into the milk, but we have no certain knowledge of any excepting iodide of potassium, which has been found in the milk of women by Peligot as well as by Herberger.

As in the case of the blood, it will hardly be irrelevant if after this notice of the normal and abnormal constituents of the milk,

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[*] Journ. f. pr. Chem. Bd. 47, S. 130—134.

[†] Guy's Hospital Reports. New Series, vol. i., p. 328.

we enter into a brief consideration of the differences presented by this fluid when examined in relation to its general physiological bearings.

Colostrum generally appears as a turbid, yellowish fluid, similar to soap and water, having a viscid consistence and a strongly alkaline reaction. It passes more rapidly into lactic fermentation than normal milk, and it also constantly exhibits an excess of solid constituents both in women and animals, as we learn from the investigations of Simon, and of Chevallier and Henry. According to the last named observers, this augmentation is most marked in the casein (in cows, asses, and goats). In women this increase principally affects the milk-sugar (according to Simon). Henry, however, finds much less sugar in the colostrum, and Simon less casein. Although a microscopical investigation and external appearances would seem to show that colostrum contains less fat, the contrary is proved by the results of most analyses. The colostrum is richer in fat than the corresponding milk. The cause of this striking phenomenon may perhaps depend upon the quantity of fat contained in the granular masses (corps granuleux). The colostrum contains moreover from two to three times more salts than the milk.

The colostrum of women yields, according to Simon, 17·2% of solid residue, and women's milk on an average 10·9%. The colostrum of the cow gives 16·0%, and the milk of the same animal from 14 to 15%; the colostrum of the ass yields, according to Chevallier and Henry, 17·16%, but asses' milk only 8·35%. The colostrum of the goat, according to the same analysis, contains 35·9%, and the milk 13·2%.

Women's milk is in general of a more bluish white colour than that of the cow or other animal, and is likewise sweeter in flavour. It has a strongly alkaline reaction, and turns acid less readily than other kinds of milk. Its specific gravity varies between 1·030 and 1·034, and it contains from 11 to 13% of solid constituents, amongst which there is on an average 3·5% of casein, and from 4 to 6% of sugar of milk. The casein in women's milk is less readily and completely precipitated by acids and by rennet, according to the concurring testimony of Simon and Clemm; the coagulum is also in general somewhat gelatinous and not so dense and solid as that of cows' milk, and therefore more easily digested by the child's stomach. The butter of women's milk is supposed to be richer in olein than that of cows' milk.

Cows' milk is in general of a pure or somewhat yellowish white colour. Its specific gravity varies, according to Simon, between 1·030 and 1·035, and according to Scherer, between 1·026 and 1·032. It contains on an average 14% of solid constituents (varying between 12·9 and 16·5%). It contains more casein than women's milk (see vol. i., p. 383) and somewhat more butter, but less sugar of milk and far more salts, although this increase principally affects the insoluble salts belonging to the casein, with whose augmentation they are likewise increased.

Mares' milk is white, tolerably thick, with a specific gravity varying from 1·034 to 1·045 (according to Clemm it is 1·0203). It contains 16·2% of solid residue, a small proportion of casein (1·7%), but a large amount of fat (6·95%), and a considerable quantity of sugar of milk (8·75%).

Asses' milk, which is of a white colour and sweeter than cows' milk, has a specific gravity which fluctuates between 1·023 and 1·035. It contains from 9·16 to 9·53% of solid constituents, of which from 1·6 to 1·9% is casein, from 12·1 to 12·9% butter, and from 6·8 to 6·29% sugar of milk; it is, therefore, far poorer in casein and butter than cows' milk, but richer in sugar of milk. This milk likewise very readily becomes acid, and easily passes into vinous fermentation.

Goats' milk is white, of a faintly sweetish taste, and a peculiar odour. Its specific gravity is in general about 1·036. It contains from 13·2 to 14·5% of solid constituents, amongst which from 4·02 to 6·03% are casein, from 33·2 to 42·5% butter, and from 4·0 to 5·3% sugar of milk. It is therefore poorer in casein than cows' milk, contains nearly the same, or perhaps a somewhat larger quantity of fat, and much more sugar of milk. When coagulated, the casein forms a dense mass.

Sheep's milk is thickish, white, and of an agreeable odour and taste. Its specific gravity varies between 1·035 and 1·041. It contains 14·38% of solid constituents, amongst which 4·02% are casein, 4·20% butter, 5·0% sugar of milk, and 0·68% salts. It appears from the single analysis instituted by Chevallier and Henry to contain somewhat less casein and butter, and more sugar of milk than cows' milk.

The only carnivorous animal whose milk has been analyzed, is the *bitch*, and her milk, according to the investigations of Simon, Clemm, Dumas, and Bensch, is somewhat thick, and on heating it becomes much thicker, even if it does not perfectly coagulate. When the animal has been kept on vegetable food, the milk is neutral, or has a faintly alkaline reaction. When animal food has been given, the milk exhibits an acid reaction, and has a specific gravity varying from 1·033 to 1·036. It then contains from 27·46 to 22·48% of solid constituents, of which from 8 to 11% are casein, and from 6·84 to 10·95% butter, besides a small quantity of sugar of milk. On mixed food bitches' milk contains more butter and also more sugar of milk. It is a singular circumstance, that on evaporating this milk, its sugar is found to be converted into grape-sugar (glucose), and the solid residue attracts a large quantity of oxygen from the air (Bensch). The ash sometimes contains upwards of 93% of insoluble salts.

Although there can be no doubt that the *nature of the food* exerts an influence on the composition of the milk, it has not been shown in what manner this affects the individual constituents. From the experiments made on bitches, it would appear that a vegetable diet renders the milk richer in butter and sugar; while the solid constituents are augmented when a sufficient quantity of mixed food is given. Peligot found the milk of an ass most rich in casein when the animal had been fed on beet-root, whilst it was richest in butter when the food had consisted of oats and lucerne. Fat food increases the quantity of the butter. Boussingault found the milk of a cow richer in casein when the animal had been fed on potatoes, than when other food was taken. Reiset found that the milk of cows which were at grass was much richer in fat than when the animals had stood all night in their stalls without food, but Playfair found on the contrary that the quantity of butter in the milk increased during the night as much as during their stall-feeding, but that the quantity of butter in the milk was considerably diminished by the motion of the animals in the fields—an observation which agrees more closely than Reiset's with every-day experience. Hay that has been cut and collected in a dry summer, yields a milk which is richer in butter than hay which has been cut in a wet season.

It follows from the experiments made by Simon on the milk of a woman who was suckling, that this fluid undergoes gradual alterations during the period of lactation. For while the quantity of the butter remains nearly the same, the casein increases as the child becomes more fully developed, at the same time that the sugar of milk gradually diminishes. The insoluble salts are increased simultaneously with the casein.

The alterations experienced by the milk from deleterious substances, mental and physical affections, and diseases, have been so imperfectly investigated, that we can scarcely be said to know anything in relation to this subject. Herberger found that the milk of cows having the murrain, was richer in potash, and had a colostrum-like appearance. The milk becomes more watery in almost all morbid affections, and is then also especially poor in butter. In febrile affections it is frequently very acid.

Almost every experimentalist has adopted his own plan of *analysing the milk,* but as scarcely any methods before Haidlen's can lay claim to accuracy, it is unnecessary to give a critical notice of them, and we will here simply draw attention to the difficulties which appertain to the quantitative analysis of milk, more than to that of many other animal fluids. These difficulties extend, however, to nearly all of its individual constituents, and mainly depend upon the following conditions:—While undergoing the process of evaporation, the milk becomes covered by the well known casein-membrane, which during rapid evaporation is often broken by vesicles of steam, by which a portion of the fluid may spirt out and be lost. It is extremely difficult to dry the milk completely after it has once undergone evaporation, and indeed almost impossible unless a very small quantity of this fluid has been employed for the determination of the solid residue; for the dry casein, when penetrated by fat, forms a crust which is impermeable to water, and even to vapour. The casein is not perfectly thrown down from the solution by means of acetic acid (see vol. 1, p. 383), since some portion may be extracted by alcohol as well as by water. When acetic acid is employed, the acid enters into combinations with alkalies, and augments the alcoholic extract in a manner which it is not easy to control, or even to estimate. The fat cannot be perfectly extracted from the simple residue of the milk, however long the latter may have been submitted to the action of ether. On evaporating sour milk, the sugar is in part converted into grape-sugar, or into an uncrystallizable syrup-like sugar. When milk is exposed to a warm temperature, the so-called extractive matters are formed in considerable quantity. It is more difficult to incinerate the residue of the milk than that of many other fluids. We are not yet able to make even an approximate determination of the investing membranes of the milk-globules.

Dumas and Scherer suggest, as a method for determining the casein with every possible accuracy, that the milk, after it has been evaporated in a water-bath or in a vacuum with sulphuric acid till it is nearly dry, should be treated with a little acetic acid, and then extracted with ether, alcohol, and water. In my opinion Haidlen's method (see vol. i., p. 383) is in many respects preferable to this, for the treatment of milk with definite quantities of sulphate of lime presents great advantages for evaporating and drying the fluid, and for determining the quantity of fat, independently of the circumstance that the casein is insoluble in all menstrua. Milk which has been treated with chloride of calcium, a solution of sulphate of lime, or, according to Haidlen's method, with dried gypsum, may easily be evaporated without experiencing any loss by the formation of vesicles of vapour; while at the same time the residue readily admits of being very perfectly dried, and then easily pulverised. Ether readily and completely extracts the fat, but alcohol does not remove any casein, either by boiling or after the fluid has cooled. A different method must, however, be adopted for the determination of the solid residue, the salts, and the aqueous extract. The best mode of proceeding is to evaporate from 1 to 3 grammes of milk in a flat platinum basin, either in a vacuum or in a water-bath, and then to dry it in an air-bath at + 120°, or in a vacuum with the aid of a small sand-bath heated to 120°. The ash is best determined when a portion of well-dried residue is burnt in a platinum crucible with the co-operation of oxygen. Scherer's method is the only one by which the aqueous extract can be determined with any degree of accuracy.

We would refer to the observations already made (at p. 297 of vol. i.), for the method of obtaining a quantitative determination of the milk-sugar; simply remarking here, that acid milk must be neutralised before its evaporation, in order to obtain the milk-sugar in a crystallised state.

Dumas* observes that the milk-globules remain upon the filter when the milk has been treated with a concentrated solution of chloride of sodium. I have not been perfectly successful in this experiment, even when I have used freshly drawn milk.

Attempts have been made to invent instruments and methods for determining with promptness the goodness of the milk, in order to detect some of the numerous modes of adulterating cows' milk usually practised in large towns. These instruments, which are termed *galactoscopes* and *galactometers*, are designed to furnish an average determination of the quantity of fat contained in the milk, since the goodness of this fluid for ordinary purposes is estimated according to the amount of fat which it contains. The best known of these instruments is the galactoscope invented

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* Arch. gén. de Méd. Vol. suppl. 1846, p. 180.

by Donné,* which consists of two tubes that may be pushed into one another by means of a fine screw, each tube being closed at the opposite extremities by a plane of glass. The determination is made by ascertaining the thickness of the milk-stratum, through which the light of a taper may be detected; the opacity of the milk being usually regarded as a test of the quantity of fat contained in it. Areometric determinations, such as Jones, Chevallier and Henry, as well as Quevenne, have proposed for the determination of the density, and consequently of the goodness, of the milk, frequently fail in their object, while Simon's suggestion of employing a solution of tannic acid, of known strength, which precipitates butter and casein from the milk, may in many cases be open to deceptions. Moreover, Lampérierre's† method of comparing the density of fresh milk with that of milk which has been filtered through paper, does not meet all the requirements of the case.

We are still very deficient in accurate determinations of the *quantity of this secretion* in women, but it must necessarily differ in accordance with the various relations of nutrition in the female while suckling. In women, the bodily constitution, the nature of the food, external relations, temperament, &c., must obviously influence the quantity as well as the composition of the milk. The quantity of the milk is, moreover, dependent upon its consumption, for in the early period of lactation, less milk is drawn from the breasts than subsequently, when the infant requires a larger amount of nutriment. Lampérierre determined, by means of the apparatus described in p. 333, the quantity of milk secreted in definite times by a large number of women, and found, as a mean for each breast between 50 and 60 grammes in the course of two hours If we were to assume that the secretion of milk proceeds at an equal rate during the twenty-four hours, then (taking 55 grammes as the mean) a woman might discharge 1320 grammes of milk in twenty-four hours from both breasts; according to this view, and assuming the mean weight of the female body to be 60 kilogrammes, there would be secreted every twenty-four hours during the period of lactation 22 grammes of milk for every 1000 grammes of weight.

We may calculate with tolerable accuracy the quantity of milk secreted by milch cows: according to the experiences of agriculturists, which coincide pretty closely with the results which Boussingault obtained in his experiments on the effects of different

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* Compt. rend. T. 17, p. 588—592.

† Op. cit.

kinds of food, a cow yields on an average 5½ litres, or about 6 kilogrammes of milk in twenty-four hours; since on an average a cow weighs 580 kilogrammes, there are thus 10·4 grammes of milk secreted for each 1000 grammes weight of the animal.

With regard to the *origin* of the milk and of its constituents, we must refer to our observations in the third volume on secretion in general. We need here only especially remark, that we cannot assume, as Chevreul and other chemists and even ourselves formerly did, that the constituents of the milk exist pre-formed in the blood. If we only adhere to the chemical view of the case, this much at all events seems established, that the presence of the leading constituents of the milk has not yet been recognised in the blood: we have already sufficiently shown, in p. 381 of the first volume, that all those reactions and phenomena from which it has been inferred that casein exists in the blood, either afford no certain proof that this is the case, or are altogether founded on error. The same is the case with the milk-sugar, which has never been recognised with certainty in the blood; the sugar of the blood, which we have especially found in the contents of the hepatic veins, and which C. Schmidt has detected in the whole mass of the blood, is fermentable; the sugar discovered by Scherer in the muscular juice, the inosite, is certainly not capable of undergoing fermentation, but in its other physical and chemical properties it differs essentially from milk-sugar; hence we may regard it as in the highest degree probable that no milk-sugar exists pre-formed in the blood, even if we do not deny that its augmentation or diminution in the milk is very dependent on the nature of the food. If these facts favour the view that the sugar is formed in the mammary glands, the pre-existence of certain constituents of the butter in the blood is by no means opposed to it: for if we assume that the capillaries of the mammary gland allow of the passage of the fats in a different proportion from that in which they are contained pre-formed in the blood, as is quite possible from the phenomena which have been observed in transudation, it is obvious that these capillaries are perfectly impermeable to the cholesterin, which is so abundant in the blood, and transudes so readily; for no cholesterin is found in the milk. On the other hand, it is very questionable whether true butyrin is contained in normal blood. Moreover, the salts do not pass into the milk in consequence of simple transudation; for on comparing the salts of transudations with those of the milk, we find that the chlorides do not preponderate to nearly the same extent in the latter as in the former, but that the potassium-compounds and phosphates are present in the milk in even larger quantities than in the blood-corpuscles: the preponderance of the insoluble phosphates in the milk-ash has been already specially noticed. But if we compare the soluble salts of the milk-ash with those of the intercellular fluid and of the blood-corpuscles (as for instance in the cow), it seems to follow as an almost necessary consequence that the blood-corpuscles take part in the formation of the milk, at all events in so far as the salts are concerned.

As when we treat, in the third volume, of the process of secretion, we shall fully enter into the histological and physiological grounds which favour the view that there occurs a preliminary remodelling of the substances to be conveyed by the blood to the glands for secretion, we will here refer to that chapter, in which, after reviewing all the chemical results which have been described in the theory of the juices, the principle is fully established, that the main constituents of all true secretions, like those of the liver and the mammary gland, are first formed within the glandular organs themselves.

The physiological importance of the milk is so obvious, that it would be altogether superfluous to enter fully into the subject: but an accurate investigation of the influences which the individual constituents of this secretion, which Nature itself has provided as the type of normal food, exert on the infant, is of such great physiological importance, that one of the fundamental laws of physiological chemistry, the very turning point of the metamorphoses of the animal tissues generally, is based upon it. For this reason we shall enter into a full consideration of this subject when we treat of the theory of nutrition, and shall, therefore, postpone all our remarks upon it for the present.

SEMINAL FLUID.

The seminal fluid, which is secreted by the testicles, and is usually mixed with the prostatic fluid, is viscid, tenacious, opalescent, colourless (only becoming yellow on drying), of a peculiar odour, considerably heavier than water, and of an alkaline reaction; when freshly discharged it is gelatinous, but after some time it assumes a thin fluid consistence; a mucous sediment is formed when it is mixed with water; the mixture is not rendered appreciably more turbid by boiling, but alcohol induces perfect coagulation.

In animals, during the period of heat, the seminal fluid may be collected in comparatively large quantities from the vasa deferentia and the vesiculæ seminales; the latter, however, secrete an independent fluid, and hence we often find no true seminal fluid in them.

This fluid contains the most remarkable morphological elements which we meet with in the animal organism, the *seminal animalcules* or *spermatozoa.* These elements which, according to the unanimous evidence of physiologists, occur in the fruitful seed of all animals, have in most cases tolerably similar although distinguishable forms; there is a round, oval, or pyriform head, to which is attached a long filament gradually coming to a point. With regard to the dimensions of these singular formations, the head in man varies in breadth from 0·0007‴ to 0·0013‴, and in length from 0·0019‴ to 0·0025‴, while the filament or tail has a length varying from 0·0018‴ to 0·0020‴. The greatest peculiarity in connection with these structures is their apparently spontaneous motion, which for a long time led to the belief that they were infusoria; the continuous motion appears to be produced by the bending and rapid stretching of the tail from one side to the other, so that the molecule moves in a zigzag direction, following the course of its head. This power of motion is often retained for a long time if the semen be protected from evaporation, or when it is placed in tepid serum, urine, saliva, or mucus; if the seminal fluid be mixed with double its quantity of water, the filaments lose their power of motion, and become more or less rolled up (Henle,* R. Wagner†). The motion is destroyed by decomposition of the semen, by spirits of wine, a solution of opium, and strychnine; the tail then generally remains extended. The spermatozoa are not readily destroyed by putrefaction; they are dissolved by concentrated but not by dilute solutions of the alkaline carbonates; the latter solutions, on the other hand, often render them more distinct under the microscope, by dissolving the coagula or mucus occurring between them. When carefully exposed to a great heat, they leave, according to Valentin, an ash, which retains their precise form.

There are likewise other morphological elements besides the spermatozoa which occur in the semen; in addition to scattered

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* Allg. Anatom. S. 949—958.

† Lehrb. d. spec. Phys. 3te Aufl. 1845, S. 49.

epithelial scales and mucus-corpuscles, R. Wagner also found finely granular, pale, sharply outlined molecules, the *seminal granules,* which vary in size from 0·0016‴ to 0·01‴; there are also minute fat-granules and molecular matter.

The *intercellular fluid* of the semen, which derives it origin less from the testes than from Cooper's glands, the seminal vesicles, and the prostate gland, gelatinizes after its discharge; Henle regards the gelatinizing substance as fibrin, while Berzelius compares it with mucus, although he does not regard the two as identical. This substance has been named *spermatin;* it is, however, probably nothing more than basic albuminate of soda, with which it coincides in most points; the fluid does not become turbid on boiling; after evaporation, this albuminous substance becomes insoluble in water; a dilute alkaline solution redissolves the matter precipitated by the water, which is again thrown down on the further addition of concentrated solutions of the caustic alkalies or their carbonates; the solid residue of the fluid is only partly soluble in water, and partly also in alcohol; on the addition of acetic acid to the watery solution, a flocculent precipitate is thrown down, which redissolves in an excess of the acid, and is precipitable from this solution by ferrocyanide of potassium; this precipitate is soluble in concentrated nitric acid. Although all these properties coincide with those of albuminate of soda (see vol. i., p. 332), we must not hence conclude that this substance is simply albuminate of soda, but we are even less justified in assuming the presence of a special substance, spermatin, or even of ordinary fibrin.

Both the water-extract and the alcohol-extract of the seminal fluid doubtless contain albuminate of soda, as far as we can conclude from the investigations of Vauquelin; but we cannot decide whether in addition to this there are special extractive matters, as in the other animal juices, since the quantity of seminal fluid that can be collected is always too small for such investigations.

The salts of the serum may be easily recognised in the seminal fluid; we find however, that the latter contains phosphate of lime, and especially phosphate of magnesia, in preponderating quantity; we can readily convince ourselves of the presence and quantity of the magnesian salt by placing semen between two glass slips which are united by varnish (in the same manner as microscopic objects are put up), and allowing it to decompose; we then observe the separation of innumerable crystals of phosphate of ammonia and magnesia amongst the uninjured spermatozoa; many have followed Vauquelin in assuming that these crystals are phosphate of of lime, but this is obviously impossible, because the latter does not crystallize from organic solutions (and these crystals present no resemblance to apatite either in their form or in the mode of their formation). But independently of this we may readily convince ourselves, both by microscopico-crystallometric and by microscopico-chemical analysis, that these are crystals of the ordinary triple phosphate.

Vauquelin* found 6% of organic matter, 3% of earthy phosphates, and 1% of soda, and hence altogether 10% of solid constituents, in the semen.

With regard to the *analysis* of the semen, we have merely to follow the rules laid down for the investigation of the animal fluids generally; in the quantitative analysis we should, however, bear in mind, that by mixing the fresh object with a very dilute solution of ammonia, the separation of the organic matters from the actual fluid of the semen may be prevented, and hence probably a quantitative determination of the spermatozoa and other morphological elements of this secretion may be accomplished by filtration. In order to examine with accuracy the extractive matters of the semen, we should first dilute the fresh fluid with a little water, and neutralize with dilute acetic acid, and then filter, before commencing to evaporate, or to extract the residue with water and alcohol.

In a medico-legal point of view the examination of the seminal fluid is of great importance. Much attention has recently been paid (by Remak,† Bayard,‡ and C. Schmidt,§) to the characters which distinguish seminal fluid on clothes, linen, &c., from other dried fluids, and enable us to detect this secretion with certainty. The form of the spermatozoa is so characteristic, and so different from all other animal or vegetable forms, that on a microscopic examination they cannot be mistaken for any other structures. The diagnosis of semen in animal fluids, as for instance the urine, is extremely facilitated by the comparatively indestructible character of the animalcules. It is further worthy of notice that I have always found that urine containing semen very readily becomes alkaline, and that even when few animalcules are found, it throws down a mucous sediment of peculiar, finely laminated, and very

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* Ann. de Chim. T. 9, p. 64.

† Diagnostiche u. pathogen. Unters. Berlin, 1845. S. 148—171.

‡ Ann. d'Hygiène publique. 1849. No. 43.

§ Diagnostik verdächtiger Flecke. Mitau u. Leipzig, 1848. S. 42—48.

transparent flakes. Hence the diagnosis of semen, is easy in every instance in which the object can be at once examined microscopically; in that case no chemical experiments are required, which unfortunately would fail in giving decisive results. It is a more difficult matter to prepare for microscopic examination semen that has been dried on linen or other textures. We omit any mention of the method adopted by Bayard for this object, since it is too circumstantial, requires a tolerably skilful analyst, and has other drawbacks; and we shall only give the very simple method recommended by Schmidt. His first direction is that we should ascertain on which side of the texture the spots are situated, for it is here only that we should find seminal animalcules; we can detect this side by its glistening surface when the light falls upon it, while the opposed surface appears dull and has a rough feeling. We then gather together the portion of linen on which the semen is found, and suspend it in a watch-glass half full of water; after four hours we warm the fluid having previously added a few drops of ammonia, while the portion on which the spots are situated still remain immersed; we then gently rub the surface, and afterwards examine with the microscope the fluid contained in the watch-glass.

According to Schmidt, seminal spots differ from all others, as for instance, those of the lochial discharge, vaginal mucus (whether syphilitic or non-syphilitic), pus, gonorrhœal matter, nasal and bronchial mucus, albumen, gum, fat, glue, or starch, in this respect, that the seminal spots become of a pale yellow colour when kept near to the fire for one or two hours, while the form of the animalcules is not at all changed. Other substances when treated in this manner are either coloured green (as for instance, vaginal mucus) or are not changed in colour; spots caused by animal substances may be easily diagnosed, either by their morphological elements, or by the albumen which can be detected after they are moistened. No one could mistake spots of mere fat, gum, or starch, for marks of the seminal fluid.

The *origin* of the semen and its *physiological importance* belong solely to histology and physiology; and we should be encroaching too much on these departments if we were to enter more closely into these obscure subjects, on which chemistry has as yet thrown no light, and which it will probably never be able altogether to elucidate.

The Fluids of the Egg.

While investigations in reference to the egg and its morphological elements, its development, and metamorphosis, have led to the most brilliant discoveries in physiology, the composition and character of the animal egg and its constituents have met with little attention from the chemist, and perhaps not without reason, for other fields of inquiry, alike more accessible and more extensive, promised to yield a far richer harvest than could be anticipated from the investigation of this subject. An inquiry into the constituents of the egg is still deficient in those preliminary investigations, which are necessary for the cultivation of the subject in such a manner as to correspond to the general advance of science and the present stage of histological discovery. Thus, for instance, although our knowledge of the fats is undoubtedly much advanced, and has attained a certain decisive stage, we are still wholly ignorant of many of the animal fats and of their relations to the lipoids. Our physiological enquiries have, however, shown us that the fats participate largely in promoting the growth and metamorphosis of the egg. Considerable obscurity still attaches to the chemical investigation of the various matters containing phosphorus, which occur, as it would appear, with the same constancy in the egg as in the brain and spinal cord.

We have already frequently spoken of the deficiency of our knowledge of the protein-bodies. Inquirers have scarcely ventured till the most recent times to hazard a conjecture as to the presence of other non-nitrogenous matters, as for instance, sugar, in addition to the fats in the fluids of the egg.

Under the term "fluids of the egg," we also usually include those fluids which are coeval with the development of the embryo, but which we shall not take into consideration in the present place, since we treat of the liquor amnii under "Transudations," of the liquor allantoidis under "Urine," of the vernix caseosa under "Cutaneous Secretion," and of the gelatin of Wharton* under "Mucus."

As the eggs of most animals are either very small or cannot

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* [The gelatin of Wharton is the limpid fluid with which the cellular tissue, that unites the vessels of the umbilical cord with the amniotic investment, is impregnated.—G. E. D.]

readily be obtained in any considerable numbers, those of the hen and of the carp are almost the only ones which have hitherto been examined. Since, according to Gobley's investigations,* the constituents of the eggs of both classes of animals are almost perfectly identical, we may assume that an inference may with some justice be drawn as to the composition of the eggs of all other animals from that of the hen's egg.

It is well known that the eggs of most animals do not contain the same albuminous investment as bird's eggs, but simply a fluid corresponding to the yolk, and enclosed by a membrane. We will, therefore, begin by considering the yolk, the constitution of which we only know from our experiments on that of the hen's egg. The yolk of the hen's egg consists of a very viscid, thick, scarcely translucent fluid, which is either of a yellowish red or of a sulphur-yellow colour, devoid of odour, and of a faint but peculiar taste. When mixed with water it forms a white, emulsive fluid, imparts a blue colour to reddened litmus paper, and solidifies on boiling into a very friable mass. It coagulates in cold alcohol, and yields when shaken with ether a reddish or amber-coloured fat, whilst a viscid white mass separates.

On examining the yolk under the microscope, we find that it consists of a semi-fluid mass composed of very fine *granules* (whose diameters are too small to admit of being measured), amongst which there swim variously sized *yolk-corpuscles* and *fat-globules.* The latter are distinguished by a less intense yellow colour, and by being covered with a layer of fine granules, whilst the yolk-corpuscles are surrounded by a membrane, which is, as it were, strewn with granules. When the yolk is acted upon under the microscope by hydrochlorate of ammonia, or other neutral alkaline salts, the granules almost wholly disappear, leaving only shining and sharply defined fat-globules, together with the somewhat distorted, oval, fusiform, or cucumber-like yolk-cells. The latter also exhibit a very faintly granular investing membrane. A similar distortion of the yolk-cells may be produced by dilute acetic acid, but this does not dissolve the suspended matter. But if the yolk be acted upon by concentrated acetic acid or a dilute solution of potash, the membranes of the yolk-globules likewise disappear, whilst a very finely granular substance alone remains visible, together with yellow-coloured fat. The yolk-globules behave, therefore, precisely the same as the milk-globules (see vol. i., p. 384), the only

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* Compt. rend., T. 21, p. 766—769; Journ. de Pharm. et de Chim., 3me Sér., T. 11, p. 409—417, et T. 12, p. 513; Journ. de Chim. Méd. T. 6, pp. 67—69.

essential difference being that the fat may be completely extracted from the yolk, even without the application of acetic acid, potash, hydrochlorate of ammonia, &c., although this may certainly be more rapidly effected by the application of hydrochlorate of ammonia or similar means. When we examine the yolk under the microscope, after the fat has been as far as possible removed by ether, we find that the minute granules are no longer scattered, but conglomerated into larger masses or aggregations, which are in a great measure dissolved by hydrochlorate of ammonia, acetic acid, and caustic potash, leaving only very fine, scarcely perceptible granules and flakes, which impart to the fluid a general opalescent or whey-like appearance.

I made numerous experiments, eight or ten years ago, on the constitution of the fluids of the egg, and the changes they undergo during the period of incubation, but deferred the publication of my observations, because the state of science at that time did not furnish the means of replying to the questions which I had propounded. I have unfortunately been prevented from repeating these experiments, which I the more regret, as the early observations of a mere beginner, conducted by means of the imperfect methods then in use, are but ill adapted to aid in criticising Gobley's recent experiments, which undoubtedly call for a rigid scrutiny in respect to several special points.

We are unable to determine the constitution of the spherical, cell-like fat-corpuscles of the yolk, as we have as yet neither the mechanical or chemical means necessary for the complete separation of the intercellular fluid.

They contain, as far as we are at present able to determine, scarcely anything but fat; which, however, is intermixed with the phosphorised matters of the yolk-fat. Such, at all events, seems to be the case, if we may judge by the following experiment. On repeatedly shaking the yolk with ether, we find that the portions of fat first extracted contain little or no substance yielding phosphoric acid, while those portions which have been the latest extracted by shaking the yolk with ether yield, on incineration, a very large quantity of the superphosphates of the alkalies and of lime. This difference in the quantity of phosphorus contained in the different portions of the fat is not observable when the yolk has been previously treated with hydrochlorate of ammonia, acetic acid, or potash. If the investing membranes of the yolk-globules were completely impervious to ether, this substance, when pure, would only extract fat free from phosphorus, whilst hydrochlorate of ammonia and similar substances would extract a fat containing phosphorus. (Even the milk-globules are not entirely impermeable, and are distorted by ether, although less fat is abstracted from them than from the yolk-globules when acted upon under similar relations.)

The pigments of the yolk form, together with the non-phosphorised and phosphorised fat, a principal part of the contents of these cell-formations, in which I have been unable to trace a nucleus or anything analogous to such a structure; at all events, when the yolk-cells have been treated with hydrochlorate of ammonia, they are invariably found to acquire a more intensely yellow colour than the fat-globules which have no investing membranes. They certainly are generally much larger than the latter, and must, on this account, also appear more highly coloured: some of the fat-globules are, however, wholly devoid of colour. According to these observations, the yolk-globules must occupy an intermediate place between the milk-globules and the blood-corpuscles; approximating most nearly to the former in their abundance of fat, and to the latter, in the quantity of phosphoric acid which they contain, and in their ferruginous pigment.

Since we are as yet unable distinctly to define the differences existing between the *chemical constituents* of the yolk-globules and those of the intercellular fluid, we will merely take a general view ot the respective elements of the yolk.

We have already spoken (in vol. i., p. 364) of *vitellin,* the most important albuminous constituent of the yolk. We did not then venture to depart from the ordinary view which regards the vitellin as a special kind of protein-body; but yet, however averse we are from making any assertion in reference to the supposed identity of similar bodies, we cannot withhold our opinion that the so-called vitellin is nothing but a mixture of albumen and casein. The amorphous, dark granules of the yolk consist of pure casein free from alkali, but which is as rich in phosphate of lime as ordinary casein. The true intercellular fluid of the yolk contains no casein, and simply dissolved albumen which is poor in alkali. It must be observed in the first place that it would be incorrect to maintain that the vitellin is coagulated by ether; for on repeating the experiment (as we have often done) of shaking the fresh yolk with ether and water, we find that under the fatty and yellow-coloured stratum of ether, there is formed a white and somewhat viscid mass, which has erroneously been regarded as coagulated vitellin. When these flakes are collected on the filter, after the removal of the fat and the ether, and are rinced as long as the fluid which passes through the filter exhibits any opalescence on being heated, there will remain a mass perfectly similar to the casein prepared according to the directions of Rochleder and Bopp, (see vol. i., pp. 379, 380,) and which contains in addition to the true casein some portion of albumen which is very poor in salts. This albumen will be precipitated by diluting the yolk-fluid with water, precisely as we observe in the case of white of egg and blood-serum. This substance possesses all the properties ascribed to casein (vol. i., p. 374), as we find from its behaviour towards acids and alkalies, and the alkaline, earthy, and metallic salts. We would simply observe that this substance dissolves even in very dilute solutions of hydrochlorate of ammonia, chloride of sodium, sulphate of soda, &c., leaving only a small residue (consisting of a little fat and of the investing membranes of the yolk-globules,) which renders the fluid opalescent. Acetic acid renders this solution very turbid, and boiling has a similar effect in a less degree. The substance separated by boiling is the albumen, which had been precipitated by the dilution of the yolk with water, and which has been again dissolved by the hydrochlorate of ammonia, &c., at the same time with the casein. All these concurring similarities between casein and the substance of the yolk, would not, however, have led us to regard this substance as casein, if it did not further possess the property so peculiarly characteristic of casein, of *being completely coagulated by rennet.* Thus, for instance, if rennet be added to this substance when dissolved in an extremely dilute solution of hydrochlorate of ammonia or soda, a dense casein-like coagulum will be formed in about two or three hours, at a temperature of about 30° C. As the sugar must have been entirely removed by washing, it cannot be supposed that this substance can in any way have contributed by its metamorphic action to the formation of this coagulum. One hundred parts of this substance in the dry state yielded 5·044 of ash, which consisted almost exclusively of earthy phosphates and carbonates.

In characterising as casein this substance, which has hitherto been considered to be of a special nature, we do so with the reservation that this identity must be only conditionally accepted until we have better means of establishing the presence of casein, more especially as we know, on the one hand, that casein itself is probably a mixture of several substances (containing here, as in the milk, at all events the investing membranes of fat-cells), while, on the other hand, we can gain little or no information from elementary analyses as to the difference or identity of protein-bodies.

I found 13·932% of such casein in 100 parts of yolk-fluid (precipitated by acetic acid from a solution of hydrochlorate of ammonia). The quantity of matter insoluble in the solution of hydrochlorate of ammonia (the investing membranes) amounted only to 0·459%.

The *albumen* of the yolk is contained in the fluid that is obtained by washing the casein which is insoluble in pure water; on boiling, it coagulates in flakes—a proof that nothing is contained therein but an albuminate, since in all other properties it resembles ordinary albumen, and is neither precipitated by acetic acid, nor coagulated by rennet. Of albumen of this nature, which is soluble in pure water, I found 2·841% in the fluid of the yolk; while of such as remained undissolved with the casein, and was only quantitatively determined after the precipitation of the casein by acetic acid, there was 0·892%. Prout found 17%, and Gobley 15·76% of vitellin in the yolk; this vitellin consisting of a mixture of casein, albumen, and investing membranes.

In addition to the above named protein-bodies, we find in the yolk both of fishes' and birds' eggs, a number of substances soluble in ether which are fats, or, at all events, on decomposition, yield acid and neutral fats, and contain in solution two pigments. The whole amount of these substances soluble in ether was found by Prout to be 29%, and by Gobley to be 30·468%, while I found on an average, as much as 31·146%. Sulphur has not been found in the yolk-fat either by Gobley or myself: neither the alcoholic solution of the yolk-fat, nor the water in which the fat has been warmed, reddens litmus.

In the examination of these fats, the first substances to notice are *olein* and *margarin,* whose quantity Gobley estimates at 21·304%.

It has been generally assumed the *cholesterin* is present in the yolk, and Gobley has even determined it quantitively, and found that it amounted to 0·438%. The evidences of its presence are, however, not at all decisive, even though the fusing point of the unsaponifiable fat obtained by Lecanu from egg-oil coincides with that of cholesterin, being 145° C. At all events, I have never been able to convince myself, by a measurement of the angles of the crystals which have been assumed to be cholesterin, or by any other means, that this lipoid was actually present: the crystalline tablets of this substance form, for the most part, not rhombs, but compressed parallelopipeds, whose angles are different from those of cholesterin; while the cholesterin-tablets generally present re-entrant angles, in these elongated tablets the acute angles are obliquely truncated. These crystals separate on gradual evaporation from the ethereo-alcoholic solution in feathery groups. They fuse more readily than those of cholesterin. The circumstance of their appearing to dissolve readily in cold alcohol, when they are still mixed with yolk-fat, would afford no proof of their non-identity with cholesterin, since it is a well-known property of the latter to dissolve freely in cold alcohol, in the presence of oily fats and soaps.

I am still doubtful whether *margaric* and *oleic acids* are contained in fresh yolk-fat; they may be unquestionably detected in it after exposure for some time to the air. Gobley considers that both these acids, together with glycero-phosphoric acid, are formed by the decomposition of an indifferent matter to which he has recently applied the term *lecithin.*

This *lecithin* has not yet been obtained by Gobley in an isolated and perfectly pure condition: it separates from the ethereal extract of the dry yolk, on the evaporation of the ether, in the form of a *matière visqueuse,* to whose investigation Gobley attaches a very great value, although most other fats, when similarly treated, yield a physically similar, although chemically very different *matière visqueuse.* I have been unable to discover any peculiarity in it; for all oleaginous fats yield, under favourable conditions, a similar mass, which consists essentially of margarin with a little olein. It is, however, true that the substance which contains the phosphoric acid occurs in that portion of the fat which first separates from the ethereal solution during evaporation. This substance, mixed with olein and margarin, and likewise with another matter, to which Gobley has applied the term *cerebrin,* is, according to his later researches, a perfectly neutral body, which, when treated with mineral acids or alkalies, both in its aqueous and alcoholic solutions, and even when the access of atmospheric oxygen is excluded, yields glycero-phosphoric acid, together with oleic and margaric acids. If in this process an organic be substituted for a mineral acid, the same action takes place, but less readily. Gobley found 8·426% of lecithin in the yolk of egg.

Cerebrin is obtained by treating the *matière visqueuse* with alcohol and an acid, and allowing it to stand undisturbed: it then separates as a white, soft mass, which corresponds with Fremy's cerebric or oleophosphoric acid: it also is neutral, contains nitrogen and phosphorus, swells in water like starch, and fuses at a high temperature: in its isolated state it is insoluble in ether, dissolves readily in alcohol, and combines freely with metallic oxides; if it be again dissolved in spirit of wine, it loses phosphate of lime, and reddens litmus.

We shall treat more fully of these substances when we consider "the brain and spinal cord;" and, in order to avoid unnecessary repetition, we shall postpone to that chapter a notice of our own experiments and observations.

Two *pigments* were discovered by Chevreul in the yolk—a yellow and a red one; both may be extracted with cold alcohol; the red one, which contains iron, is less readily soluble in ether than the yellow one, in which that metal is not present: when perfectly freed from fat, they appear to be all but insoluble in ether; neither of them has, however, been carefully examined.

Whether the organic acid which occurs in the yolk is *lactic acid*, is very doubtful; at all events, its presence is by no means established from the little that Gobley tells us on the subject.

Although Gobley has convinced himself that the constituents of the yolk which contain phosphorus are not in combination with ammonia, he yet assumes that *hydrochlorate of ammonia*, to the extent of 0·034%, is present in that fluid.

With regard to the *mineral substances*, we find in the ash of the yolk the ordinary salts of animal substances, but they occur in very different proportions from those in which we ordinarily find them. The compounds of potassium preponderate considerably over those of sodium, and, according to Poleck,* the chlorides are entirely absent; but, on the other hand, Rose and Weber† have more recently found that, at all events, some chloride of sodium (namely, 9·12% of the inorganic matters) can be detected in the yolk, if the organic matters have not been destroyed either by carbonisation or by incineration. Only monobasic phosphates can be discovered in the ash prepared according to Rose's method, and in this Poleck found from 66·7 to 67·8% of phosphoric acid, and Weber 70·92%; a little peroxide of iron (1·45% of the ash), and a small quantity of silica (0·55% of the ash) were also found in the yolk-ash. If we call to mind the composition of the corpuscles, we cannot fail to be struck with the great analogy that

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* Pogg. Ann. Bd. 79, S. 155—161.

† Ibid. p. 398—429.

exists between the nature of the salts occurring in the blood-cells and in the yolk; and we shall almost immediately see that, on the other hand, the composition of the salts in the white of the egg approximates in a similar manner to that of the salts of the serum.

We repeat that Gobley has found precisely the same substances, in almost the same proportions, in the eggs of fishes, which, like those of most animals, consist only of yolk, and are not surrounded with a special layer of albumen like birds' eggs.

In thirty hens' eggs I found 466·2 grammes of yolk; hence, an egg contains, on an average, 15·54 grammes of yolk; while Poleck obtained 427·361 grammes from twenty-nine eggs, according to which an egg would contain 14·75% of yolk. The amount of *water* in the yolk of fresh eggs is liable to considerable variations; it fluctuates from 48 to 55%. The *inorganic matters* in the yolk amounted, according to Poleck, to 1·523%.

We will here add, for facility of comparison, the quantitative relations of the *albumen* or *white* of hens' eggs. In thirty eggs I found 690·3 grammes of albumen, or, on an average, 23·01 grammes in each egg; Poleck found 719·742 grammes in twenty-nine eggs, and hence, on an average, 24·8 grammes in one. Moreover, the quantity of *water* in the white is very variable, fluctuating between 82 and 88%. On an average, I found 13·316% of solid constituents in the fresh white. The *inorganic constituents* amount to from 0·64 to 0·68% of the white; according to Poleck, to 0·65%. In the dried residue I found, on an average, 3·042% of fusible ash.

In the ash of the white the *soluble salts* preponderate considerably over the *insoluble*, while in the ash of the yolk the reverse is the case; the excess of the soluble salts in the ash of the albumen principally depends on the considerable quantity of chlorides, which amount to 50·45% (or according to Poleck to 41·92% of chloride of potassium and 9·16% of chloride of sodium). Soda, in combination with acids, occurs in the white in far greater quantity than in the yolk, (amounting in the former, according to Poleck and Weber, to 23·04, and in the latter to 5·12, or at most, to 5·70%); while the proportions of the potash-salts are exactly reversed, (for in the white we have 2·36, and in the yolk 8·60, or even 8·93% of potash.) Phosphoric acid is only present in small quantity in the ash of the white, amounting to 4·83%; but carbonic acid (from 11·6 to 14·05%) and a little sulphuric acid (from 1·40 to 2·63%) are also present. Silica occurs in almost the same quantity in the ash of the white (0·49%) as in that of the yolk, but the peroxide of iron is present in smaller quantity (from 0·34 to 0·44%), and so also are the lime and magnesia (there being 1·74% of the former and 1·60% of the latter); while in the ash of the yolk the earths are six or seven-fold increased, with a great preponderance of the lime, there being 12·21% of lime and 2·07% of magnesia. All these relations point to a determinate object in the distribution of the inorganic matters amongst the cells and the intercellular fluid of the animal body—a point of view which we shall find to be highly important in the consideration of the history of development.

We may readily convince ourselves of the presence of *carbonates* in the white of fresh eggs, by placing a little of this substance under the microscope, and adding acetic acid; we may then often perceive an extraordinarily great development of gas. The quantity of these pre-formed carbonates appears, however, to be very variable, and is probably dependent on the longer or shorter time during which the egg has been exposed to the air; it is possible that the carbonic acid obtained from the atmosphere may abstract a portion of the base from the albuminate of soda.

Free *gases* are contained both in the white and in the yolk, as in all animal fluids.

According to my analyses, fresh white of egg contains 12·274%, and the dried white 92·293% of *albumen* (determined in accordance with the rules laid down in vol. i., p. 339). We must refer to vol. i., p. 335, for a notice of the difference between the albumen of the egg and of the blood-serum.

The white of egg is by no means free from *fat*, although this substance is only present in extremely small quantity. On examining fresh white of egg under the microscope, we discover at intervals small granules, with three or four projecting teeth or points, which are obviously composed of margarin. If further we extract dried white of egg with ether, we sometimes, but not always, obtain a light azure solution; the fat which remains after the evaporation of the ether consists of olein and margarin, but also contains oleate and margarate of soda, if any alcohol has been present in the ether which has been used: it is precipitated from its alcoholic solution by acetate of lead; when isolated and incinerated, it leaves an alkaline ash which effervesces with acids.

We have already seen (in vol. i., p. 290) that the white of egg ordinarily contains normal *sugar;* from the determinations which have hitherto been made, it appears that in the dry residue of white of egg there is about 0·5% of sugar (as calculated from the carbonic acid developed after the induction of fermentation).

The number representing the *extractive matters* of the white after the deduction of the fat, the sugar, and the salts, is not large; I found 3·143% in its solid residue.

It is worthy of notice, that a little albuminate of soda passes over into the alcohol-extract as well as into the water-extract, if we do not previously neutralise the white, and hence we may readily obtain an apparently larger quantity of extractive matters; the acetic acid, in combination with the alkali of the alcoholic extract, should consequently be deducted in the determination of the extractive matters.

Although the white of egg is a substance that falls under our daily observation, there does not as yet exist any good *analysis* of it; for certain precautionary measures are requisite for its examination, which have not been sufficiently attended to. The gelatinous white, as we obtain it from fresh eggs, is not merely an albumen or an albuminate of soda swollen with water, together with some adhering fat and an admixture of soluble substances, but it likewise contains insoluble membranous parts; we here refer not only to the chalazæ, but also to the delicate, textureless, only faintly granular membranous structures which cross the white in various directions, and so inclose it that, even after its careful removal from the egg, it always retains the appearance of a tolerably consistent mass. These delicate membranes possess the same refractive power as the white that is inclosed within them; and hence they do not become visible till after the addition of water. It must not, however, be supposed that all the flakes which become separated on the admixture of water and white of egg, are merely these previously invisible membranes, for the albuminate of soda of the egg, like that of the blood-serum, separates by strong dilution with water into an albuminate rich in alkali, and into albumen poor in alkali; the latter increases the insoluble part of the albumen that has been modified by water. We may readily convince ourselves on this point, by the addition of a neutral alkaline salt, as for instance, chloride of sodium or hydrochlorate of ammonia, to albumen which has been thus treated, and has become almost white and opaque from the separated flakes; a very great part of the turbidity then disappears, and we can now perceive, on a microscopic examination, that the portion which still remains undissolved consists merely of the prolongations of the chalazæ and the membranous parts. Hence, in order to determine with accuracy the quantity of the true *albumen* in the white of egg, a quantity of the latter (perfectly fresh, and weighed in a closed vessel) must be carefully triturated in a mortar; the watered white of egg is then to be poured into a cylindrical glass, and to be diluted with fifteen or twenty times its quantity of water. Without this very free dilution, the albuminous solution can hardly be filtered, and even then it will often not pass through the filter in summer at a high temperature, when formations of byssus and vibriones so readily occur. After the whole of the fluid has been placed upon the filter, it is adviseable at once to treat the residue with an aqueous solution of hydrochlorate of ammonia, and then to thoroughly wash it. The hydrochlorate of ammonia not merely dissolves the albumen which was precipitated by the water, but it likewise has the effect of allowing the whole of the albumen to coagulate on subsequently boiling the filtered fluid; it supersedes the acetic acid that is generally recommended, since there are formed chloride of sodium and albuminate of ammonia, which latter parts with its ammonia on boiling, perfectly coagulates, and forms a coagulum which may be readily collected on a filter.

The *fat* of the white of egg, like the extractive matters and the sugar, must be detected and quantitatively determined by the methods which have been already described in their appropriate places.

The presence of pre-formed *alkaline carbonates* can only be determined by the same method which has been already described as applicable to the blood and to transudations (see p. 328); when they have been determined, we may readily find a means of calculating the quantity of alkali in combination with albumen. Unfortunately, however, in consequence of the varying proportions in which the alkaline carbonates, and the alkali in combination with albumen, exist in different eggs, the determinations that have been made are so various, that as yet we have not succeeded in determining a definite ratio of the alkali to the albumen, or of the alkaline carbonates to the albuminate of soda.

The analysis of the yolk also presents its difficulties, some of which cannot be altogether overcome. The yolk-corpuscles are the less easily separated mechanically from the rest of the fluid, in consequence of the simultaneous presence of free granules of undissolved vitellin and fat-globules. I have found the following to be the best method of proceeding with the analysis; as in the examination of animal fluids generally, we must first ascertain the amount of solid residue and of salts; the latter must, however, only be determined by Rose's method, since by the application of a strong red heat for the purpose of incinerating, we should unquestionably lose a portion of phosphoric acid. To determine with any degree of accuracy its albuminous constituents, the uninjured yolk must naturally be in the first place freed from adhering white, by repeated but quick rincing. The fluid of the yolk, which must now be allowed to escape from its membrane and very readily dries, must be weighed and shaken with ether as long as it continues to impart the faintest yellow tint to that menstruum. The remaining watery albuminous fluid then forms a white semi-solid mass; this must be shaken with water, which takes up a great part of the albuminous matter; its quantity is determined by boiling; the fluid which is poured away from the coagulum, is evaporated, and the residue is extracted with alcohol; and the quantities of the water-extract and of the alcohol-extract are thus determined; this, however, serves only as a check for the other method, according to which the quantity of the extracts is determined from the solid residue of the whole fluid.

A large proportion, however, of the albuminous constituents of the yolk, comprising the casein and some albumen devoid of alkali, remains undissolved in water; this portion is now to be treated with a dilute solution of hydrochlorate of ammonia, by which the yolk-granules which are visible under the microscope, the casein, and the albumen that has been precipitated by water, are dissolved. The solution of these substances is heated, which precipitates the *albumen;* and the casein-containing fluid, after the separation of the albumen by filtration, is then carefully treated with dilute acetic acid, which precipitates the *casein*; or conversely, the casein is first thrown down by acetic acid, and the albumen is subsequently precipitated by boiling, after the neutralisation of the acetic acid by ammonia. In order, however, to remove all protein-matters from the fluid, it is necessary that the filtered fluid should be evaporated to dryness, and the residue freed from hydrochlorate and acetate of ammonia by rincing with cold water. It is only further necessary to refer to the rule laid down in p. 223, that all albuminous substances, after being thoroughly washed with water, should also be treated with boiling spirit, in order to remove any adhering matters which are insoluble in water, but soluble in alcohol. This is especially necessary in the case of vitellin, since this substance, when obtained in the above mentioned manner, is seldom altogether free from fat.

The white flakes that are insoluble in the solution of hydrochlorate of ammonia, and consist for the most part of the *membranous investments* of the yolk-globules, must be washed with distilled water to remove the hydrochlorate, and must then be dried and weighed.

The *sugar* must be determined from the alcohol-extract (after it has been freed from fat), either by fermentation, or by Fehling and Trommer's method.

Lactic acid, even when it is actually present, occurs in such small quantity, that we can scarcely hope to be able to determine its amount.

To determine the quantity of the *fat* and of the *phosphorised matters,* we must evaporate the yolk-fluid and dry it at 110°, before we extract it with ether. An accurate separation of the different substances soluble in ether is at present impossible; we shall, however, refer somewhat fully to the methods of separating and quantitatively determining the phosphorised substances of the fats, of the salts of the fatty acids, and of certain lipoids, when we treat of the cerebral and nervous tissues, since the phosphorised matters there fall especially under our notice. We have already (in vol. i., p. 247) indicated the general method of distinguishing the neutral fats from the fatty acids, and of separating them from each other.

We refrain from offering any remarks on the *physiological importance* of the individual constituents of the yolk, since this subject will be fully noticed in the history of development. It is certainly no rash conclusion to believe that in the egg the animal substrata are deposited in a condition ready for the formation of cells and tissues, and to base our view of the metamorphosis of food into organised matters on the constitution of the egg and the development of the embryo in it. We should hence be guilty of useless repetition if we were, in this chapter, to discuss the importance of each individual constituent of the egg in relation to the history of development.

MUCUS.

THERE is scarcely any animal fluid within the entire range of the theory of the juices that has been so little investigated, in a scientific point of view, as the mucus; and the reasons of this are sufficiently obvious. In the first place, the expression "mucus" has a very vague signification; for although the proposition has been advanced, that the secretion of the mucous membranes alone is to be regarded in the light of mucus, we yet find, that under certain conditions there is secreted in the animal organism a limpid, viscid juice, having all the characters of mucus, without however being secreted from a true mucous membrane with the so-called mucous follicles. We need here only refer to the mucous contents of certain cysts which yield, according to the investigations of Virchow* and Rokitansky,† all the reactions which have been regarded as characteristic of normal mucus. Several colloid abnormal as well as normal structures, as, for instance, the gelatin of Wharton, become converted into a fluid, which cannot be distinguished by any reaction from normal mucous juice. Another and still more important ground for the silence of chemists in reference to the constitution of mucus is, that the normal mucus is always so filled or interspersed with morphological elements, that it cannot be obtained in a purely chemical condition. In the present state of analysis, we are unable to separate these structures from the actual mucous juice, and we cannot prosecute a satisfactory chemical investigation of this substance, except in those rare cases in which a mucous juice is secreted which contains few of these cells, either from their original scarcity, or from the facility with which they may incidentally be removed from the fluid. These cases, as we have already observed, are rare, and the question even then remains, whether the substance we are investigating is perfectly identical with the mucous juice. May we venture, on the strength of some few coincident reactions, to pronounce upon the identity of juices springing from such different sources, whilst we think ourselves justified in separating globulin from albumen, and vitellin from casein? Can we re-establish, by

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* Verhandl. der Gesellsch. f. Geburtshülfe in Berlin. 1848. Bd. 3, S. 203.

† Zur Anatomie des Kropfes. Wien, 1849, S. 11, reprinted from first volume of Denkschriften der mathem. naturwiss. Classe d. kais. Akad. d. Wissensch.

means of alkalies, certain combinations with albumen and fibrin, which will exhibit all the physical and many of the chemical properties common to mucus? What differences, moreover, exist in the properties and characters of perfectly genuine mucus, which has originated from different mucous membranes? We do not here refer to the acid or alkaline reaction, or to the admixture of different cells, but simply to the different capacity for exerting a digestive action with acids on animal substances. But even if the chemist should succeed in overcoming all these difficulties, his labours would be of no avail, in consequence of the impossibility of obtaining the fluid in a normal condition; for this juice is secreted in such small quantities on all the mucous membranes, as long as they continue in a normal state, that only the merest traces of it can be obtained. We also know how easily the mucous membranes may become diseased, and how much the mucus differs in these cases from the normal secretion. Daily experience shows how rapidly the number of the so-called mucus-corpuscles increases with the slightest irritation of the mucous membrane; and we know from the researches of Julius Vogel, that an irritated mucous membrane secretes not only such corpuscles, but also an albuminous, coagulable matter, however much it may be disposed to form true transudations and exudations. A proper consideration of all these circumstances furnishes an excuse for the neglect of chemists towards a subject whose investigation is so desirable both in a chemical and a physiological point of view. Then, moreover, the question regarding the mode of formation of this juice has not been decided by physiologists; for whilst in most mucous membranes, special organs, the so-called mucous follicles, have been regarded as the source of the mucus, there are also mucus-secreting membranes, which are entirely devoid of these follicles,—as, for instance, those of the antrum Highmorianum, the frontal and sphenoidal sinuses, the cavity of the tympanum, the ovula Nabothi, the synovial sacs, and finally, abnormal formations, as hygroma, cysts, &c. Hence the source of the mucus cannot be referred, or at least, not exclusively, to the glandular organs of the mucous membranes. Tilanus* drew attention to the circumstance that all these membranes are invested with an epithelial layer, and that the epithelial cells are probably integral components of the mucous juice, which must therefore stand in a causal connection with these bodies. But it would appear from the observations of Virchow† and Roki-

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* De saliva et muco, spec. inaugur. Amstelodami, 1849, p. 56—75.

† Arch. f. path. Anat. u. Physiol. Bd. 1, S. 115.

tansky,* that the colloid matter of cysts of the thyroid gland, and of the liver, kidneys, and ovary, may be converted into a substance very similar to, or even identical with the mucus, no epithelium being present in it. In the same manner as permanent cartilage may be converted into glutin, the gelatin of Wharton is readily converted into mucus (Virchow).†

We will now briefly consider the various histological elements which are blended with normal and abnormal mucus.

Normal mucus is never free from the *epithelium* of the mucous membrane from whence it has originated, and may, indeed, be said to consist almost entirely of epithelium, which appears to be only held together by means of a pellucid juice. This is as much the case with the mucous membranes which are invested with pavement epithelium, as with those which exhibit the cylindrical or ciliated structure; the cilia of the latter are, however, in general thrown off, so that we can rarely find perfect ciliated epithelium even in abnormal secretions.

According to the assertions of several observers, *mucus-corpuscles* do not occur in normal mucus; but some of these bodies may always be found on carefully examining the expectoration from the mouth, the normal mucous cloudy sediment in the urine, or the solid excrements. Although the mucus-corpuscles, which have justly been regarded as abortive epithelial cells, exhibit no distinct differences, either in a morphological or even in a microchemical point of view, from the ordinary pus-corpuscles; yet it cannot be denied that it requires the aid of water, or acetic acid, to bring into view the nuclei both of the normal and sparingly dispersed mucus-corpuscles, and of those corpuscles which are secreted from the mucous membrane during catarrh; in this case, however, the nuclei present one or more fissures. The mucus in blennorrhœal discharges contains little epithelium, and consists almost solely of mucus-corpuscles which are suspended in a greater or less quantity of viscid intercellular fluid. No essential difference can be observed between it and pus, in so far as either the collective fluid or the cells are concerned.

In the so-called exudative, or croupous inflammations of the mucous membrane, we constantly find *fibrinous coagula*, which frequently bear the impress of the cavity, or canal, from which they have originated; and at other times appear in the form of

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* Ueber d. Cysten. Wien, 1849, S. 20, reprinted from the first volume of Denkschr. d. math. naturwiss. Classe d. kais. Akad. d. Wissensch.

† In a Private Communication.

small, fibrous flakes, interspersed with mucus- or pus-corpuscles. These bodies occur in the expectorated mucus in diphtheritis, pneumonia, Bright's disease, dysentery, and similar affections of the mucous membranes. In these cases *blood-corpuscles* are also found to be present.

When the inflammation of the mucous membrane has ceased, and an exudation of a croupous nature is no longer separated from the canal, certain changes generally occur, which in the ordinary course of the process give occasion to the formation of pus-corpuscles, and during the slower resolution of the exudation, tend to the development of the *inflammatory globules* or *granular cells.* Histology shows us that these morphological elements vary considerably in size and form. We would here, however, draw attention to the fact, that a species of such granular cells occurs in the mucus, and more especially in the bronchial mucus, without having been preceded by any croupous inflammation of the mucous membrane. (They occur, for instance, in the tenacious, thick mucus, which is expectorated in the chronic bronchial catarrh of aged persons.) Under such circumstances, there is only a small quantity of mucous juice in addition to the granular cells and masses, and rarely any other morphological elements; the granules of the cells are in general much larger than those of the usual inflammatory globules, and resemble the nervous tissue in their strong refracting power. In many respects they bear a resemblance to the *corps granuleux* of the milk. In addition to these, there occur concentrically striated corpuscles, which often present the size and form of the granules of potato starch, and greatly resemble them. They are probably identical with *Hassal's corpuscles,* found by Henle* under similar conditions.

It is well known that such sputa are often of a grey, or sooty colour, exhibiting in many cases steel-grey, highly glistening cilia, which are visible to the naked eye. These cilia may be readily isolated by a needle or scalpel, and when brought under the microscope the appearance they present is simply that of closely crowded granular cells of the kind above described, except that they exhibit no trace of pigment-molecules, or of black, or dark coloured masses. I do not know how to explain this phenomenon, except on the supposition that all the light has been absorbed by the densely crowded and strongly refracting cells, in the same manner as we observe that many metallic sulphides which appear black when observed in masses by the naked eye, exhibit nothing

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* Zeitschr. f. rat. Med. Bd. 7, S. 411

more than a mass of strongly refracting globules, when seen in a finely comminuted form, under high magnifying powers. The black, sooty colour has frequently been ascribed to lamp-smoke, or to finely comminuted coal-dust, which has been inhaled; but although I have never been able to detect anything of the kind, I would not, on that account, deny that under certain conditions, as, for instance, in colliers, smiths, &c., coal-dust may become mixed with the bronchial mucus. Many of the experiments instituted in relation to this subject are hardly worthy of confidence.

Free *fat* occurs in almost every kind of mucus, either in the form of vesicles or of very minute granules, and either in mere traces or in large quantities.

Molecular or elementary granules are seldom absent from the mucous juice, but they are more decidedly observable when the mucus has originated in a diseased structure, as in tuberculosis or cancer, but more especially in typhus, in which the milk-coloured sputa appear, when seen under the microscope, to be enveloped, as it were, in a veil of very fine granules. We still more frequently remark the presence of such granules in intestinal mucus, owing to the favorable conditions afforded for the separation of these molecules by the decomposition of albuminous substances.

Intestinal and cellular formations of various shape and size, (Valentin's exudation-cells,) as well as similar elements from the solitary and agminated glands which are usually found within the mucous membranes, are of very frequent occurrence in morbidly secreted mucus.

Vibriones, microscopic fungoid growths, and similar organic particles, can only be considered as of incidental occurrence.

Amongst the chemical constituents of the mucus, *mucin* occupies the first place. The presence of this substance imparts to the mucus its most important properties; but, unfortunately, it has never yet been completely separated from the above described morphological substances, neither has it been obtained pure and free from other chemical organic or inorganic matters. This may be one of the causes why different mucous juices often behave very differently towards individual solvents and reagents.

Mucin is generally considered as insoluble in water, and as distributing itself in a finely comminuted state through the fluid in which it swells; occasionally, however, as Scherer* has observed, a mucus is found which actually dissolves in water, and may be

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* Ann. d. Ch. u. Pharm. Bd. 57, S. 196—201.

separated by filtration from the morphological substances. The mucous juice does not coagulate when exposed to heat, but becomes in some instances more thinly fluid and more nearly similar to a true solution. Alcohol precipitates the mucin from the fluid in flakes and threads, while dilute acetic acid precipitates it in the form of viscid flakes; if it occurs as a gelatinous mass, it is converted by the same acid into white threads or fibres. The flakes and fibres are insoluble in extremely dilute acetic acid, but they dissolve when treated with the concentrated acid and with the aid of heat. The mineral acids behave in a similar manner, precipitating the mucin when diluted, and again dissolving it very readily when employed in a concentrated state. Mucin, on the other hand, dissolves very readily in dilute alkalies, but much less speedily in concentrated solutions. Acetic acid precipitates a larger quantity from dilute than from concentrated alkaline solutions, which is owing to the circumstance, that mucin, if not entirely soluble, yet admits of being reduced to a gelatinous state in solutions of alkaline salts, when not too dilute. Acetate of potash prevents the mucin in these cases from separating perfectly into flakes. Gelatinous mucus is frequently, as it were, coagulated by water, which causes it to become denser, and to lose its translucent, gelatinous character. This change is very probably owing to the abstraction by the water of the alkali or alkaline salts to which it partially owes this gelatinous condition. Ferrocyanide of potassium does not throw down mucin from the alkaline or the acid solution. (When, as is frequently the case, the mucus is precipitated from the acetic-acid solution by ferrocyanide of potassium, albumen or some similar protein-body is probably present with the mucin.) When, on the other hand, mucus is boiled with concentrated acetic acid, it will be very copiously precipitated by ferrocyanide of potassium. Hot concentrated nitric acid colours it yellow, while it is changed to a blue colour when heated with hydrochloric acid and exposed to the air. Tannic acid or basic acetate of lead gives rise to a considerable precipitate from the aqueous, weak alkaline mucous solution, whilst nothing beyond a faint turbidity is induced by alum, chromic acid, bichloride of mercury, neutral acetate of lead, and other metallic salts.

Several elementary analyses of mucus have been instituted, but they can scarcely afford us any aid in judging of the composition of the mucin, since the epithelium has been included in the substance examined. Scherer, who has alone succeeded to some extent in exhibiting a preparation in any degree fit for an elementary analysis, found, as the mean of three experiments, 52·1% of carbon, 6·97% of hydrogen, 12·82% of nitrogen, and consequently 28·11% of oxygen. No sulphur was found, but there was 4·114% of white ash, which contained some alkaline carbonates, in addition to a tolerably large quantity of phosphate of lime.

Scherer obtained this mucus from a sac between the trachea and the œsophagus, which was probably an abnormally dilated bursa mucosa. The mucus could be filtered when strongly diluted with water, so that the morphological substances admitted of being removed. The mucin was precipitated from the solution by alcohol, and was then repeatedly boiled in alcohol and ether.

We have already referred to the observation of Julius Vogel, which admits so readily of confirmation, that the mucus secreted in catarrhal irritation of the mucous membrane exhibits a varying quantity of *albumen.* There are also cases in which the normal mucus may contain albumen; and if we include under the head of mucus, as indeed we almost necessarily must, the mucous investment of the stomach, which is intermixed with the gastric juice, we have a mucous juice, which constantly contains albumen (Buchheim).* I have seen the contents of the ovula Nabothi rendered turbid by heating. Tilanus always found albumen together with mucin in the synovia within the joints. The mucous fluid of colloid cysts contains varying quantities of albumen, as we learn from the reactions obtained by Virchow and Rokitansky.

The peculiar substance named *pyin,* which has frequently been found by Güterbock in pus, has been regarded by many observers as a constant constituent of mucus, and even as identical with mucin (Eschholtz).† The erroneous character of such an opinion may, however, be readily seen on comparing the properties ascribed to the pyin found in pus with those of mucin.

Fat occurs only in very small quantities in normal mucus, although the quantity increases in proportion to the occurrence of albumen and larger quantities of mucus-corpuscles. Nasse‡ found 6·25% of a semi-solid, yellowish white fat in the solid residue of the normal nasal secretion, whilst the same mucus contained only 4·448% of solid constituents.

The mucus likewise contains *extractive matters* soluble in water and alcohol, but they have not been very carefully examined. The quantity of these substances is no doubt increased by the glandular secretions which are mixed with the mucus in the stomach and

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* Dissert. inaug. Leips., 1845.

† Rust's Magazin. Bd. 10, S. 160.

‡ Journ. f. pr. Ch. Bd. 29, S. 59.

intestinal canal, and in this manner the intestinal juice and mucus have frequently been identified with certainty. But the difference between the mucus and the glandular secretion effused upon the intestinal mucous membrane, ought to be strictly kept in view. We have already spoken (at p. 118) of the intestinal juice.

The *free acids* frequently found in the mucus are included amongst the extractive substances. Andral* maintains that true, pure mucus is always acid in a normal state; but although this assertion may be true, it has not been proved, nor indeed would it be very easy to do so; for as we are not acquainted with any entirely pure mucus, which may possibly be wholly free from any reaction on vegetable colours, we may assert, in reference to every mucus which exhibits an alkaline reaction, that this property may be owing to certain admixtures, consisting either of pure transudations from the blood or of special glandular secretions. As may be readily conjectured, no careful investigation has as yet been made in reference to the nature of the free acid which occurs, amongst other instances, in the secretions of the mucous membranes of the mouth and the urinary bladder.

In considering the quantity of the *alkalies* contained in mucus, we must especially bear in mind that no inconsiderable portion of the soda is combined with true mucin, as was observed by Berzelius† in the secretion from the mucous membrane of the nose, and by Scherer in the abnormally generated mucus above referred to. Nasse also found alkaline carbonates together with carbonate of lime in the ash of the normal nasal secretion.

Mucus is very rich in *alkaline chlorides,* of which Berzelius found 0·56% in fresh nasal mucus, and Nasse 13% in the dry residue of similar mucus, which, however, contained no cells.

Nasse found some alkaline *sulphates and phosphates,* together with earthy phosphates, in the ash.

Berzelius found 6·63% and Nasse 4·448% of solid constituents in the nasal mucus, and Scherer 11·299% in the above described abnormal mucus. The latter observer likewise found 7·6% of ash in 100 parts of the solid residue.

Unfortunately, however, no attention has been paid in these analyses of the normal mucus to the relation existing between the potash and the soda. Yet the establishment of this relation is not wholly devoid of importance in the solution of the question, whether the blood-corpuscles take part in the preparation of the mucus as they do in that of most other secretions, or whether the mucus is

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* Compt. rend. T. 26, p. 650—657.

† Lehr. d. Chem. 4 Aufl. Bd. 9, S. 531.

formed solely from the constituents of the blood-plasma. I know of only one analysis of the kind suited to throw light on the subject, and this yielded more potash and less soda in the ash of the mucus than in that of the blood-serum; but as this mucus had been secreted during an acute catarrh, and besides being very rich in young cells (mucus-corpuscles), contained also some granular cells, it does not afford any conclusive evidence.

The *method* of analysing mucus would be very simple, if it were not wholly impracticable, in most cases, to separate the true *mucin* from the *cells* which are intermixed with it. It is only in a few rare instances, as in the case investigated by Scherer, and already referred to, that the morphological elements can be collected on the filter by mixing the object with a large quantity of water, and rendering it capable of being filtered by repeated and continuous shaking. The mucin, however, instead of being distributed through the water, is in many instances converted into an apparently coagulated condition, this being more especially the case with catarrhal bronchial mucus, which becomes shrunk by the abstraction of the alkaline salts which had previously caused the mucus to present a swollen appearance. When the mucin is not soluble in water, the only method of determining it even in an approximate degree, is to filter the substance after it has been digested with highly diluted ammonia. Unfortunately, however, the mucin which has been dissolved by the alkali passes very slowly through the filter, in consequence of the obstruction presented by the gelatinous swollen epithelium. In many cases, therefore, this method proves insufficient for the separation of the mucin from the above described morphological elements. If we succeed in removing the epithelium by filtration, the mucin may be precipitated from the neutral or weakly acid solution by spirit, and from the alkaline solution by dilute acetic acid; after this, the precipitate must be washed with hot spirit, and after being dried at a temperature of 120°, must again be washed with hot water, in order to remove all the mineral and organic substances which are insoluble in spirit. The waters employed in rinsing must then each be strongly concentrated, and immediately evaporated with the spirituous solution filtered off from the mucin, while the residue is extracted with ether, alcohol, and water.

When *albumen* is present with the mucin, which indeed it very generally is in the large quantities of the substance necessary for such investigations, the difficulty of the analysis is greatly increased. If the mucin were insoluble in water, which appears to be never altogether the case, the separation of the soluble albumen from the insoluble mucin might be very easily effected; but this is by no means the case, for the swollen, gelatinous, or apparently coagulated mucin only gives up the albumen to the water with difficulty, and after a long time. Hence it is necessary, if we would desire to attain a comparatively successful result, to distribute the mucus repeatedly in water, and after suffering it to form a deposit, to pour only the clear fluid upon the filter, repeating the process until the filtered fluid no longer exhibits any opalescence on heating; for the insoluble mucous residue cannot be collected on the filter until the albumen has been completely removed. The quantity of the latter substance may be determined by the ordinary rules, and a further separation of the mucin from the epithelium may then be effected by means of diluted alkalies.

If the substance named *pyin* occur in the mucus, or if the latter contain a substance not coagulable by heat, but precipitable by acetic acid, although not again soluble in an excess of this acid, the albumen, in case the fluid was not alkaline, must *previously* be precipitated by boiling, and its quantity determined, after which the pyin-like substance may be separated from the filtered fluid by acetic acid. In case, however, the mucous fluid is alkaline, this substance must first be precipitated by acetic acid, and then washed for some time, in order to remove any albumen that may have been precipitated from the solution by acetic acid; and after the filtered fluid has been carefully neutralised by ammonia, which generally imparts some degree of turbidity to it, it must finally be boiled.

The quantitative determination of the remaining organic and mineral constituents of the mucus may easily be conducted by following the rules already given.

We are necessarily unable to form any estimate of the *quantity* of mucus secreted by the different mucous membranes; and it would seem sufficient to draw attention to the view advanced by Valentin, that the secretion separated from the surface of many of the mucous membranes must be regarded as exceedingly small, or even absolutely nothing in the normal state. It can only be regarded as the result of special or general irritation, when any considerable quantity of mucus is separated from an apparently healthy mucous membrane;—a view which seems to derive confirmation from the circumstance, that normal mucus can never be obtained from the living body in quantities sufficient for chemical analysis, but must be scraped away from the mucous membrane of animals immediately after they have been killed. The liability to error presented by such means is too obvious to need further comment. It is probable that the secretion is seldom perfectly normal when present in excess in morbid affections of the mucous membranes, and that it is generally mixed, in these cases, either with a transudation or exudation. This is shown both by the microscopico-mechanical and the chemical investigation of morbidly secreted mucus.

We have already observed, in the beginning of this chapter, in reference to the *origin* of the mucus, that the seat of the formation of this fluid is not limited to the mucous follicles, for we have already noticed several mucous membranes in which there was no appearance of any such glandular organs. Some facts, indeed, seem to warrant the conclusion, that the formation of mucus is not limited to a definite spot, or associated with any definite tissue. The conversion of Wharton's gelatin into a substance perfectly similar to mucus in respect to its physical and chemical properties, the gradual transition of the colloid mass of many cysts into perfect mucus, and its occurrence in many exudations proceeding from serous membranes, are facts which cannot be lost sight of in our consideration of the origin of mucus. Tilanus has drawn special attention to the circumstance, that epithelial structures are always present wherever there is true mucus. This observation might lead to the assumption, that the formation of mucus is connected with the development of certain cells, that is to say, that its production occurs simultaneously with the development of certain morphological elements. Two views here present themselves for our consideration; one of which is, that the albuminates of the liquor sanguinis become decomposed, under certain hitherto unknown conditions, into the substratum of the epithelial cells and into mucus, whence the latter substance might in some respects be considered as a secondary product of this cell-formation, so that the mucous juice in the mucus would hold the same relation to the epithelial cells as the spirituous fluid does to the yeast-cells in a mixture which has undergone fermentation. The other view, which seems to be supported by numerous observations made by Scherer and Virchow,* refers the origin of the mucus to a partial disintegration of the epithelial cells. All who have followed Frerichs in his observations on the metamorphosis of the cells within the gastric juice, or who have examined them by the microscope in the preparation of artificial gastric juice, will easily comprehend the gradual solution of the gastric cells

* In a Private Communication.

and their conversion into a mucous fluid. Such a conversion of cells into a mucous substance would, therefore, at all events not be wholly without analogy. Scherer and Virchow, however, go still further, and advance the opinion, based upon several pathologico-histological observations and chemical experiments, that certain colloid substances, and others adapted for the formation of urine, may be converted into mucus under certain conditions which still remain to be explained, and even without any cell-formation; and hence they regard the latter mode of development as associated with the existence of colloid or cartilaginous substances. This view is supported not only by the absence of epithelial structures in many mucus-containing cysts, but more especially by the frequently noticed conversion of the gelatin of Wharton into perfect mucus. It appears to us still to require accurate chemical experiments, to decide which of these two hypotheses deserves the preference. The elementary analyses which were made by Scherer on a single variety of mucous juice, unfortunately do not enable us to decide the question, both because the atomic weight could not be determined, and because we are still entirely deficient in an accurate analysis of the epithelial cells, the colloid substance, &c. It remains for us to hope that the investigating powers of men like Scherer may before long enrich science with the knowledge necessary for elucidating a subject which is so intimately associated with the advancement of physiology.

The localities in which mucus occurs clearly demonstrate that it is especially designed to serve as a protecting medium to all the parts which are placed in a reciprocal connection with the outer world (Joh. Müller).

Cutaneous Secretions.

Although in a certain point of view we may regard the epidermis, the nails, hairs, feathers, and scales, as products of the secretion of the skin, these objects will find a more appropriate place in the third volume, when we treat of histological chemistry. We shall, therefore, here only notice those two well-known secretions, the sebaceous matter and the sweat.

The *sebaceous matter* is secreted by those innumerable glandular structures, the *folliculi sebacei,* which are distributed over the whole skin; they are racemose, branching glandules, with flask-like or pear-shaped secreting vesicles (the saccules or acini) and a very narrow neck. There are simply two anatomical points to which we would here refer, seeing that they have a bearing on the further consideration of the sebaceous matter. The first of these points is, that these sebaceous glands are always entirely embedded in the non-fatty corium, and, although they secrete fat, are never found lying in the fatty subcutaneous areolar tissue; the second is, that the great majority of these glands are grouped around the roots of the hairs, and that their narrow mouths open into the hair-follicles; it is only on the *nymphæ,* the *glans penis,* and the inner membrane of the *præputium,* that we find sebaceous glands independently of the presence of hairs; the glands on these parts have, however, a somewhat different formation, the acini or saccules being more rounded and grouped in a mulberry-like form. We might here also mention the racemose Meibomian glands, and the coiled and twisted tubular ceruminous glands, since we shall, in the present chapter, consider their secretions, in so far as our chemical knowledge of them at present extends.

Although the secretions of the above named glandular organs by no means have a perfectly identical composition, and indeed probably, to a certain extent, contain very heterogeneous constituents, yet, in regard to many of their physical and chemical relations, they are at least as nearly allied as the transudations which were considered in a previous chapter. In order as much as possible to include the comparative physiology of the subject, we shall, at the same time, notice the composition of castoreum, which has been shown by E. H. Weber* to be essentially nothing more than the secretion from the innumerable preputial folds of the penis and clitoris of the beaver.

In all these secretions, without a single exception, we find a larger or smaller number of morphological elements: all these glandular vesicles and ducts are invested with a fine cellular epithelium, and hence, on a microscopic examination, we find *epithelial cells* in all these secretions; we often, however, find more pavement epithelium from the external skin than delicate cellular structure from the interior of the gland.

In most of these secretions, and especially and invariably in those of the Meibomian and ceruminous glands, we find peculiar, oval, angular, or roundish *cells,* from $\frac{1}{200}$th to $\frac{1}{140}$th of a line in diameter, which, in addition to a pale nucleus with nucleoli, con-

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* Ber. d. k. sächs Gesellsch. d. Wiss. Bd. 2, S. 185—200.

tain minute, dark, and clearly defined granules, and a few distinct fat-globules.

The sebaceous glands, like the mucous follicles, when in a state of inflammatory irritation, produce those primary cells to which we apply the terms *pus-cells*, mucus-corpuscles, &c. These cells are present in small quantity after even the slightest irritation of the skin and of the follicles in question, but especially in the thoroughly puriform fluids which are secreted in inflammatory affections of the external auditory meatus and of the Meibomean glands, in balanitis, in acne, and in similar cutaneous disorders, which for the most part have their seat in the hair-follicles.

The minute animal described by G. Simon*, the *acarus folliculorum*, is commonly found in the normal secretion of the sebaceous glands, as well as in the so-called *comedones*.

An *albuminous substance* is contained in all the secretions of the above named glands; it cannot, however, be easily exhibited in the soluble form, since, in accordance with the method by which alone we can analyse these solid fatty matters, it is always separated in the insoluble state; hence we cannot determine whether it is most similar to casein or to albumen; it is obviously a protein-body from its behaviour with acetic acid and ferrocyanide of potassium, with concentrated nitric acid, hydrochloric acid, &c. Esenbeck,† who had an opportunity of examining a mass contained in a very distended hair-follicle, found in the dry substance 24·2% of this albuminous substance; I ‡ found 4·0% of it in the vernix caseosa of a tolerably full-sized fœtus, 5·6% in human smegma præputii and 2·9% in that of a horse, 2·4% in the semi-solid mass obtained from the fresh pouch of the beaver (after drying), and 5·8% in Canadian castoreum.

Fats and *lipoids* constitute the principal part of these secretions: the ether-extract in the above mentioned case of Esenbeck's amounted to 26·2%, while in the vernix caseosa I determined it at 47·5%, in human smegma præputii (collected after several operations for phimosis) at 52·8%, in that of the horse at 49·9%, in the fresh castoreum of a German beaver at 7·4%, in Russian castoreum at 2·5%, and in a specimen from Canada at 8·249%.

Of the *saponified fats*, olein and margarin are found in considerable quantity in the ether-extract; but in none of the secretions which I have examined, including the cerumen, was there a trace

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* Müller's Arch. 1842, S. 218.

† Gmelin's Handb. d. Ch. Bd. 2, S. 2155.

‡ Ber. d. k. sächs. Ges. d. Wiss. Bd. 2, S. 200—208.

of butyrin or of butyric acid to be detected, although, as we shall presently see, this acid is very frequently secreted by the sudoriparous glands.

Of *lipoids* I found in the smegma præputii a little cholesterin, besides a body soluble in ether and hot alcohol, and very similar to cholesterin, but not crystallizable; in the vernix caseosa I found only this substance, and could not detect any cholesterin.

No *phosphorised fatty bodies* were found either in the vernix caseosa or in the preputial secretion.

The alcoholic extract of these secretions consists for the most part of the *margarates and oleates of potash, soda, and ammonia;* here also no alkaline butyrates can be detected; the ammonia-soaps preponderate considerably in the preputial secretion.

In addition to the soaps, the alcohol-extract contains only a little organic matter which does not admit of further determination, unless a substance peculiar to a special secretion or some incidental matter happen to be present, of which we shall speak further presently.

Berzelius* obtained from the *cerumen* a fat which was soft, white, opaque, easily fusible, devoid of action on litmus, and when treated with potash, yielded an extremely fetid soap, which, on the addition of hydrochloric acid, deposited the fatty acids in the form of a white powder; these acids did not readily rise to the surface of the solution, and fused at about 40°.

Vauquelin found that the fat of human *hair* was oleaginous and coloured, and that it contained sulphur.

The fatty *sweat* which adheres to undressed wool consists, according to Vauquelin,† chiefly of a potash-soap; while, on the other hand, Chevreul,‡ who has more recently examined it, found non-saponifiable fats containing neither sulphur nor nitrogen, one of which fuses at 60°, while the other is fluid at 15°; to these two fats he gave the respective names of *stearerin* and *elaerin.*

I found that the *alcohol-extract* in the vernix caseosa amounted to 15·0%, in the human preputial smegma to 7·4%, and in that of the horse to 9·6%.

The resinous constituents of the castoreum soluble in alcohol still require a more accurate investigation than they have yet received. The amount of these matters in castoreum is extremely

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* Lehrb. d. Chem. Bd. 9, S. 536.

† Ann. de Chim. T. 47, p. 276.

‡ Compt. rend. 1840. No. 16.

variable; in a fresh German specimen I found 67·7%, in a smoked Russian specimen 64·3%, and in a Canadian one 41·34%.

In all these secretions I also found small quantities of matter soluble only in water, the organic portion of which did not admit of further determination. In the vernix caseosa I found that the water-extract amounted to 3·3%, in the human preputial smegma to 6·1%, and in that of the horse to 5·4%.

That portion of these secretions which is insoluble in water, alcohol, and ether, consists for the most part of the histological structures which have been already mentioned, and likewise of hairs; at all events, so far as the vernix caseosa is concerned, through which we always find a network of *lanugo* running. From this mass we may extract the above mentioned albuminous substance, which, however, at all events, in part belongs to the cells.

We find only a small amount of soluble *mineral constituents,* namely, a little *chloride of sodium* and *hydrochlorate of ammonia,* with *phosphate of ammonia and soda. Earthy phosphates,* on the other hand, occur in considerable quantity; there being, according to my analyses, 6·5% in the vernix caseosa, 9·7% in the smegma præputii of man, and 5·4% in that of the horse.

From this sketch of the few experiments to which secretions of this class have been subjected, we may at all events draw this conclusion, that however different the position and the structure of the sebaceous glands may be, they secrete tolerably similar products.

It is sufficiently obvious that no great weight can be attached to the determinations of the *quantity of water* in these secretions; in order, however, to give some general idea of the amount of water that is present, it may be mentioned that in the vernix caseosa I found 66·98%, and John Davy* 77·87% of water, but that in the secretions of the sebaceous glands of animals living in the air, the quantity of water is far less in consequence of the continuous evaporation, although it is liable to great variations depending on external conditions.

We have now to mention a few substances which are to be regarded either as incidental admixtures or as constituents peculiar to individual secretions. Amongst these we must first mention a *bile-like substance,* which I have found in the preputial secretion of man, the horse, and the beaver: as I have been unable to find it in the vernix caseosa, in the cerumen, or the secretion of the Meibomean glands of a scrofulous child, it appears to be peculiar

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* Medico-chir. Trans. 1844, p. 193.

to the hairless sebaceous follicles of the prepuce and the glans penis. It was obtained from the ethereal extract by extraction with water, and yielded, with sulphuric acid and sugar, the most beautiful biliary reaction; that this could not be fat, is sufficently obvious from its solubility, as well as from the rapidity with which the reaction ensued; but whether the substance is identical with any of the products of decomposition of the biliary acids, is a question that must be decided by further investigations.

The *resinous constituents* of castoreum have been already mentioned. Wöhler* has shown that they contain *carbolic acid*, or *oxide of phenyl* ($C_{12}\ H_6\ O_2$), which may be detected by the blue colour it imparts to a pine-shaving saturated with hydrochloric (Runge) or nitric acid (Laurent). Since the resinous constituents of castoreum coincide in a remarkable manner with those of hyraceum (which, according to my investigations, can only be the dried intestinal excrement of Hyrax capensis), and since phenylic acid occurs in both these substances, it seems most probable that they are not products of the metamorphosis of tissue, or that they are any peculiar secretion, but merely derivatives of the resinous substances conveyed in the intestinal canal of the animal with its food.

Benzoic acid has been detected in castoreum by Saugier, Brandes, Batka, and Riegel; from certain experiments which I made on the contents of fresh pouches, I think it probable that *hippuric acid* is originally contained in this substance.

I found *benzoic acid* in the preputial smegma of a horse.

It is very doubtful whether *uric acid* occurs in castoreum, although Brandes believes that he has found it.

In the preputial secretion of herbivorous animals, there is little phosphate of lime, which seems replaced by *carbonate of lime;* this, at all events, is very abundant in castoreum. This salt may be easily recognised, by observing under the microscope the considerable development of gas which the residue, insoluble in ether, alcohol, and water, yields on the addition of acetic acid, and by noting the considerable turbidity that is induced in the fluid which is thus obtained, by the addition of oxalate of ammonia.

In fresh castoreum we can recognise with the microscope the well known crystals of *sulphate of lime,* and in the preputial smegma of the horse, the octohedral forms of *oxalate of lime.* The presence of both salts may be readily confirmed by a few microchemical experiments.

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* Ann. de Ch. u. Pharm. Bd. 49, S. 360, and Bd. 65, S. 342.

The smegma præputii of the horse, which I obtained for analysis, was of a blackish grey colour, soft and plastic like wax, and somewhat viscid when fresh; but when dried, it was hard, almost brittle, and presented a glistening fracture.

Little remains to be noticed regarding the different methods of *analysing* these secretions, both qualitatively and quantitatively, in addition to the ordinary general rules, and to the special remarks on the detection of each individual constituent.

The above mentioned *albuminous substance* can be only approximately determined, since it can only be extracted by acetic acid from the residue of the matter that is left after extraction with ether, alcohol, and water; this acid, however, abstracts a little albuminous matter and a certain quantity of earthy salts from the cellular structures of the residue. I determined this matter in the following manner:—I dried the residue after its extraction with indifferent menstrua, and determined its weight; I then digested it for several hours in moderately dilute acetic acid, rinsed it, and after drying again, weighed it; the loss of weight indicated the sum of the matters extracted by the acetic acid; the acid solution was evaporated, and its residue, without any further treatment, was incinerated for the determination of the mineral matters; the weight of the ash was then deducted from the loss of weight which the residue had suffered from the acetic acid. I thus obtained the number representing the quantity of the albuminous substance contained in the secretion.

With regard to the *carbolic acid*, we have only further to add, that its presence is by no means so easily to be recognised as might be supposed from the above named reactions; for, independently of the extremely minute quantity in which it occurs in castoreum, the application of pine or fir shavings, saturated with hydrochloric acid, is exposed to certain fallacies; for the shavings of these woods, after being acted on by this acid, readily assume a bluish green colour on exposure to the sun: hence it is necessary, before applying this test, to separate the carbolic acid as completely as possible from the resinous and fatty constituents of the castoreum, which, however, in consequence of the slight solubility of carbolic acid in alcohol and ether, and its high boiling point, 187° C, is altogether impracticable when only small quantities are present.

We have nothing to add to the observations contained in the first volume, regarding the method of detecting and separating the *lipoids* and *fats, hippuric, benzoic,* and *uric acids, oxalate of lime,* &c.

We have at present no means of determining the *quantity* of matter secreted by the sebaceous glands collectively, or by special groups of them; moreover, daily experience teaches us that the amount must be very variable in different individuals and under different physiological and pathological conditions.

With regard to the *origin* of this secretion, we must bear in mind (when further investigating it) that the fat of the sebaceous glands must either be derived directly from the blood of the capillaries coiling around them, or must be formed from other matters in the cells of these minute glands; for it is worthy of notice that almost all these sebaceous glands are, as it were, rooted in a tissue which is completely devoid of fat, and do not penetrate into the fatty cellular tissue beneath the corium; the *glans penis* is almost absolutely devoid of fat. The variously refracting granules, globules, and vesicles which occur in many cells, as, for instance, in those of the external auditory canal and of the Meibomian glands, so frequently appear to represent new progressive stages of development of the same object, that we are almost led to the conjecture that the fat peculiar to these secretions is primarily formed within these glands.

These glands yield a fatty investment to the hair and cuticle; Krause* regards it as definitely established that this secretion diminishes the hygroscopical property of the horny layer of epidermis and of the hair, and that it hence checks the too rapid evaporation of moisture, and the drying up of the deeper epidermic layers and of the corium.

Under the term *sweat* we include only the fluid secretion of the sudoriparous glands, without reference to the question, whether these glands are also the sources of the gaseous transpiration of the skin or not. The sudoriparous glands are thread-like, delicate, single tubes, not communicating with one another, which originate in a blind extremity in the fatty subcutaneous cellular tissue, where they form spirally twisted coils; they then make their way through the corium and the younger epidermic layers in a corkscrew-like or serpentine course, and finally open with a considerably contracted mouth in the cuticle. These tubular sudoriparous glands are always invested with an epithelium which consists of roundish or oval-angular nucleated cells.

The sweat, as it collects in drops upon the skin of a person who is perspiring freely, is, as is well known, a colourless, very watery fluid, with a rather saltish taste, and usually communicates a

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* Handwörterb. de Physiol. Bd. 2, S. 135.

peculiar, more or less, intense odour, which varies with the cutaneous surface from which it has exuded: in most cases it has a weak acid reaction; indeed it is only sweat which has been collected from the axillæ and the feet that is often found to be alkaline.

It is very difficult to obtain a sufficient quantity of sweat for chemical analysis in order to ascertain its constituents. Thénard and other chemists have employed shirts saturated with sweat, and extracted the sweat from them by various solvents; but this is the least advisable method, since here there is always a larger or smaller quantity of sebaceous matter mixed with the sweat; perfectly clean sponges are generally used in this case in order to dry the skin which had been previously cleansed, but is again brought into a state of perspiration. In this way the above mentioned error is certainly much diminished, but it is not altogether avoided; for we still find in the sweat a very large number of epithelial scales, to which a little of the sebaceous secretion always adheres. The best method is that which was adopted by Anselmino,* who enclosed his arm in a glass cylinder that was rendered as air-tight as possible, and was thus able, in the course of five or six hours, to collect about a tablespoonful of sweat.

The sweat contains only a very small amount of solid constituents; Anselmino, whose method of proceeding is certainly the best that has been yet adopted, found that the solid non-volatile constituents varied from 0·5 to 1·25%.

The principal constituent of the sweat, that is to say, the substance which, next to the water, occurs in the largest quantity in this fluid, is, according to the experience of all observers, the *chloride of sodium*. *Phosphate of soda* is not found in sweat, and the *sulphate* only rarely (Simon†), while, on the other hand, the presence of *salts of ammonia* is very obvious (Berzelius‡); the ammonia in the sweat is not only combined with hydrochloric acid, but also with organic acids; indeed it probably exists as carbonate of ammonia in alkaline sweat.

Earthy phosphates and a little *peroxide of iron* are constantly found in the sweat; they are, however, probably dependent on the admixture of epithelial cells with the fluid under examination; it is only in consequence of the assumption that lactic acid is contained in the sweat, that it has been also assumed that phosphate of lime exists in a state of solution in it.

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* Tiedemann's Zeitschr. Bd. 2, S. 321—342.

† Handb. d. med. Ch. Bd. 2, S. 326—336 [or English Translation, Vol. 2, pp. 101—111.]

‡ Lehrb. d. Chem. Bd. 9, . 390—397.

It must still remain very doubtful whether the *fat* which is found in the sweat proceeds from the sudoriparous glands, or, whether it only depends on the admixture of a little of the secretion of the sebaceous glands. The fat of sweat that has been collected in the ordinary manner has, in point of fact, precisely the same physical and chemical properties as the fat of the sebaceous glands, as I have convinced myself by an examination of the very profuse perspiration of a woman after delivery. Krause* has, however, shown, by a very admirable experiment, that, in reality, the sudoriparous glands themselves secrete true fat (together with butyric acid, &c.) It is well known that there are no sebaceous glands on the palm of the hand or the sole of the foot; Krause removed the fat and any loose epithelial scales from the palm of the hand by ether and friction, and then covered a square inch of it with a pad of filtering paper, from which all fatty matter had been removed by ether; this pad was firmly attached to the hollow of the hand, and retained there for one night, being securely guarded from external impurities; a gentle perspiration was induced towards morning; the paper, on being submitted to the action of ether, then yielded a fat which, in addition to margarin, contained an oily matter which rendered tissue paper distinctly transparent.

We may further readily convince ourselves of the presence of *butyric acid* in the sweat, by extracting with spirit textures thoroughly impregnated with sweat—as, for instance, stockings, flannels, and other parts of the dress that have been worn next the body—and distilling the extract; we then saturate the acid distillate with potash, evaporate, and decompose the salt with sulphuric acid, when a most distinct odour of rancid butter is developed; I even succeeded in obtaining the baryta salt, but the small quantity of irregular crystals was insufficient to enable me to prove with certainty by micrometrical measurement, that the salt was butyrate of baryta. If we can form an opinion from the odour of different kinds of sweat, it is very probable that caproic and metacetonic acids, which are closely allied to butyric acid, are also present; in many diseases, especially such as are accompanied by an acute exanthematous eruption, there is often a singularly strong smell of metacetonic acid. Anselmino and Simon have also detected *acetic acid* in sweat by its smell; since this acid, if it actually occur in the sweat, is always associated with other volatile acids of this group, it cannot be determined with certainty by any of the known tests for acetic acid: it is only by experimenting with very large

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* Op. cit. p. 146.

quantities that we can form a decided opinion regarding the existence of acetic acid in sweat: we think it not improbable that it occurs there. Berzelius considers that *lactic acid* is the free acid of the sweat, and that it likewise is in combination with the ammonia; Berzelius has, however, not operated on such quantities of sweat as to have enabled him to determine this acid with his ordinary accuracy. Since, according to my investigations, the secretion of the sebaceous glands, even after saponification, yields either no volatile fatty acids, or, at most, very small quantities of them, the above mentioned volatile acids must of necessity pertain to the secretion of the sudoriparous glands.

The *extractive matters*, which afford so much annoyance to the chemist, are of course present here; from the facility with which the sweat decomposes, it is even more difficult to arrive at any definite conclusion regarding its extractive matters than regarding those of many other animal fluids. Although we cannot recognise amongst these substances any material which possesses the properties of a protein-body, a *sulphurous matter* must be contained in the sweat; for if we keep fluid sweat in a closed glass, we find that a considerable quantity of sulphide of ammonium is formed as soon as decomposition commences.

The observations which have been made by physicians regarding the qualitative and quantitative changes which the sweat undergoes in diseases are of so uncertain a character, that we must hesitate in basing any conclusions on them. Such observations and conclusions as the following,—namely, that as the sweat of persons who perspire very copiously, as, for instance, of rheumatic and arthritic patients, has a very distinctly acid reaction, therefore rheumatism and arthritis depend on a lactic-acid dyscrasia or diathesis,—might have been well spared in medicine. We need hardly observe that the increased acidity is in such cases dependent upon the concentration of the sweat by evaporation.

Anselmino maintains that he detected *albumen* in the "critical" sweat of a patient with acute rheumatism.

*Urea** has not yet been found in the sweat; but it may probably occur there in cases in which the blood is richer than usual in this substance, and in which there is a very copious secretion of sweat.

Wolff † thought that he had once detected *uric acid* in the dried sweat from the forehead of a patient with calculus.

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* [Urea has been found in the sweat of healthy persons by Landerers (see Arch. f. Chem. u. Mikros. Bd. 4, p. 196), and by Schottin, a pupil of Lehmann's, in cases of renal disease (see Schmidt's Jahrb. Bd. 74, S. 9.)—G. E. D.]

† Diss. inaug. sing. cas. calculositatis. Tüb. 1817.

Every physician must have had opportunities of observing that certain *pigments* sometimes occur in the sweat of patients; thus the body-linen of jaundiced persons who perspire freely, sometimes assumes a yellow colour. Blue and red pigments have also been observed in the sweat.

It has been shown by the experiments of Milly, Jurine, Ingenhouss, Spallanzani, Abernethy, Barruel, and Collard de Martigny,* that *gases,* and especially *carbonic acid* and *nitrogen,* are likewise exhaled with the liquid secretion of the sudoriparous glands. According to the last named experimentalist, the ratio between these two gases is very variable; thus, in the gas developed after vegetable food there is a preponderance of carbonic acid, and after animal food an excess of nitrogen; Abernethy found that on an average the collective gas contained rather more than two-thirds of carbonic acid, and rather less than one-third of nitrogen. When the process of perspiration is especially active, as, for instance, after strong bodily exercise, less gas is on the whole exhaled.

With regard to the *method of analysing* the sweat, we have scarcely anything to add to the remarks already made (in various parts of the first volume) respecting the determination of the individual constituents contained in this secretion; we must, however, especially recollect that its volatile constituents can only be accurately determined by a careful examination: and again it must not be forgotten that the sweat very easily decomposes, and gives rise to the secondary formation of ammonia.

Numerous, and undoubtedly very careful, investigations have been made regarding the *absolute quantities* of the substances which are thrown off in a definite time by the sudoriparous glands and the skin generally. We shall postpone any notice of those investigations which, from the time of Sanctorius to that of Scharling, have simultaneously included the cutaneous and the pulmonary transpiration, and have estimated their sum collectively, till we treat of the respiratory process. Cruikshank, Abernethy, Dalton, and Anselmino, attempted in various ways to determine the amount of the cutaneous secretion; the most important, however, was that which Anselmino adopted, of determining the amount of the perspiration given off by a single extremity or by a known extent of cutaneous surface, and then calculating how much would be given off by the whole surface of the body; but independently of the circumstance that the other data for our

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* Journ. de Physiol. T. 11, p. 1.

calculation depend for the most part on very uncertain assumptions, no great weight can be attached to the final result. The argument *ex parte in totum* here holds good even to a less extent than in any other case, in consequence of the unequal distribution and unequal development of the glands (as, for instance, in the axillary region); and finally, the cutaneous surface, when enclosed, can hardly discharge its functions in the same manner as when it communicates freely with the atmosphere.

The calculations founded on the very laborious investigations of Seguin* should lead us nearer to the truth, although the non-volatile constituents of the skin have not been here included in the calculation. Seguin obtained absolute numbers for the amount of matter transpired by the skin, by weighing his body in such a manner that he determined the loss of weight which the body experienced when the respiration and perspiration are unimpeded, and then compared this with the loss of weight which the body underwent when the perspiration was retained in an air-tight case. It appears from these experiments, that the mean amount of the cutaneous is to that of the pulmonary transudation as 2 : 1, a ratio to which the still more carefully conducted experiments of Valentin also lead us, if we deduce it, as Krause† has done, from the sum of the quantities of water and carbonic acid expired by the lungs in twenty-four hours, and from the loss of weight which occurs during the same period from pulmonary and cutaneous transpiration. Valentin ‡ found, by weighing at intervals of three days, that on an average his body lost 1246·93 grammes in twenty-four hours from cutaneous and pulmonary transpiration; from his measurings of the quantities of water and carbonic acid that are expired, as contrasted with the quantity of inspired oxygen, it followed that in the same time Valentin lost on an average 455·18 grammes; hence the perspiration in twenty-four hours amounted to 791·75 grammes, and the ratio of the perspired to the expired matters was as 9 : 5. Notwithstanding that the calculations founded on his experiments led to almost the same results as those of Seguin, Valentin§ regards it as altogether impossible that more matters should be eliminated by the cutaneous perspiration than by the pulmonary exhalation; I agree, however, with Krause, in thinking that the above ratio is in all probability the true one.

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* Ann. de Chim. T. 90, p. 52—88 et 413—580.

† Op. cit., p. 144.

‡ Lehrb. d. Physiol. d. Menschen. Bd. 1, S. 714.

§ Ibid., p. 582.

It appears to me that we in no degree detract from the full importance of the respiratory process, in considering that the loss of weight occasioned by pulmonary exhalation only happens to be so small because at the same time there is a great absorption of oxygen, which is not the case with the perspiration. If, for instance, we compare the quantities of the carbon and hydrogen eliminated through the lungs in twenty-four hours with the carbon and hydrogen of the perspiration (which, however, owe their oxidation for the most part to the oxygen absorbed by the lungs), the ratio becomes considerably modified and much more in favour of the pulmonary exhalation, the sum of the weights of these elements in the cutaneous transpiration being to that in the pulmonary exhalation as 24 : 14. Hence there is nothing so extraordinary in the ratio assigned by Seguin, as to induce us to doubt that it approximates to the truth.

According to Brunner and Valentin* there are about 10·4 grammes of carbon, and according to Vierordt 1·5 of hydrogen, expired every hour in the form of carbonic acid and water. If we assume that the 51·95 grammes, which is the hourly amount of perspiration, according to Valentin, consist of 0·93 of a gramme of carbonic acid (as Abernethy asserts), 0·31 of a gramme of nitrogen, and 50·71 grammes of water, there would be 0·25 of a gramme of carbon, 0·92 of a gramme of nitrogen, and 5·57 grammes of hydrogen, removed by the perspiration in an hour. Hence the separation of non-oxygenous elements through the lungs would be to that through the skin in the ratio of 11·9 : 6·75, which corresponds pretty closely with that of 24 : 14. If we compare the quantity of the oxides exhaled from the lungs with that of the oxides in the cutaneous transpiration, we find that the two quantities are almost perfectly equal; for in the course of one hour there are exhaled from the lungs 51·53 grammes of carbonic acid + water, and from the skin 51·95 grammes of the same oxides, together with nitrogen.

We possess very few, and, from the nature of the case, very inaccurate determinations regarding the quantities of the sweat which are secreted under special relations, as, for instance, during strong bodily exercise, after abundant draughts of water and being enveloped in blankets, in the vapour-bath, &c. The only observations bearing on this point to which we will refer, are those of Berthold,† which were made in a vapour-bath, and therefore

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* Arch. f. phys. Heilk. Bd. 2, S. 373—417.

† Müller's Arch. 1838, S. 177.

under circumstances in which the sweat that was thrown off could not evaporate, and also where water could not easily be given off by the lungs; Berthold found that after he had remained half an hour in the vapour-bath, he had lost a pound and a half in weight; since the carbonic acid exhaled from the lungs is nearly replaced by the inspired oxygen, we may fairly assume that an adult man in a vapour-bath loses about 25 grammes of sweat in a minute.

According to Abernethy, there are about 412 cubic inches of carbonic acid exhaled from the skin of a full-grown man in twenty-four hours.

Krause calculated that in the course of twenty-four hours there are excreted by the sweat of an adult male 791·5 grammes of water, 7·98 of organic and volatile matters, and 2·66 of mineral substances.

Physiologists have long held different views regarding the *sources* of the cutaneous transpiration, some maintaining that the whole of the cutaneous transpiration and sweat arise solely from the sudoriparous glands, while others assert that an elastic fluid permeates the epidermis. We shall revert to this subject, in so far as it falls within the scope of our inquiries, when we treat of the mechanical metamorphosis of matter.

The *importance* of the cutaneous transpiration is so obvious to every one, that we might readily believe that its objects would be sufficiently manifest; yet the most we can do is to frame hypotheses on the subject. One of the undoubted uses, although not the principal object, of the cutaneous transpiration, is to regulate the temperature of the animal body. Although there is a perfect correspondence of physical laws and physiological experiments in so far as this function of the perspiration is concerned, it has in general been somewhat over-estimated; because, on the one hand, the external temperature is almost always below the temperature of the body, and hence the evaporation of fluids is not required to cool the organism from the surface inwards, and because, on the other hand, the activity of the lungs, by which the blood is almost directly cooled, fulfils this object in a far higher degree. It is generally believed that the transpiration is the medium through which certain substances are eliminated, whose retention, in cases of suppressed perspiration, might give rise to various morbid conditions. The most superficial observer cannot fail to perceive the extremely injurious consequences that often follow even a partial suppression of the transpiration, and hence the analysis (which is always imperfect) of the chemical constituents which the skin separates, not only fails to give us any conclusion, but it might probably lead us to the erroneous view that this function of the skin may be perfectly replaced by the kidneys, for the constituents of the sweat are collectively contained in the urine. We should, however, obviously be drawing too general a conclusion, if we were led from the investigations of chemists to ascribe a less importance to the cutaneous transpiration. When we can directly refer individual groups of symptoms to affections of the peripheral nerves, induced by rapid cooling, there follows a group of sequelæ, which we cannot help ascribing to the retention of certain deleterious substances. In the present imperfect state of zoo-chemical analysis in reference to the volatile odorous matters, we may readily believe that the substances of this nature, which always occur more or less abundantly in the sweat, induce definite changes in the metamorphosis of the blood as well as in the functions of the individual organs, and thus occasion the various forms of diseases arising from chill; many, however, of the volatile matters pertaining to the materia medica and to toxicology, when introduced into the mass of the juices, even in extremely minute quantities, induce the most urgent morbid phenomena. There is no secretion—not even the very analogous pulmonary exhalation—in which we find such various and penetrating odorous substances as in the cutaneous transpiration. Strongly odorous matters, as, for instance, balsam of copaiva, musk, ether, the dead-house smell, &c., when taken into the system, are not only given off with the flatus and the pulmonary exhalation, but also by the cutaneous transpiration. Hence it would seem as if the skin, like most other organs, provided for the separation of certain peculiar matters, and thus fulfilled a special object in the economy of the animal organism.

As a natural sequence, we should here notice the pulmonary exhalation, but the positive results of the investigations that have been hitherto made in relation to this subject, are so intimately connected with those undertaken to elucidate the process of respiration, that we must run the risk of being charged with procrastination or want of clearness, if, from a love of systematic arrangement, we should boldly separate from one another investigations undertaken with a single idea.

URINE.

If there were any branch of zoo-chemistry from which physiology and medicine might reasonably have expected to reap any certain knowledge in reference to the vegetative processes in the animal body in health and disease, it was assuredly the urine. For if the physical properties and changes exhibited by this secretion, under different conditions, had even attracted the attention of the ancients, and led them to the knowledge of a number of highly significant, although unexplained facts, the subject could not fail, from its accessible nature, early to become a matter of inquiry on the revival of scientific investigation. The readiness with which the urine might be obtained, necessarily facilitated the labours of experimentalists in a greater degree than is the case with most other objects submitted to analytical investigation. Hence the early inquirers, whose attention was chiefly directed to the observation of animal phenomena, made the elucidation of this subject a special object of their investigations. Men such as van Helmont, Boerhaave, and others, who excelled in all branches of the sciences cultivated in their age, instituted several very admirable experiments with the urine; while those who aided in establishing modern chemistry, amongst whom we may instance Cruikshank, Fourcroy, and Vauquelin, have left us tolerably perfect analyses of this highly compound fluid. At the beginning of the present century, the analysis of the urine was one of the earliest investigations of Berzelius, and it still ranks, after a period of fifty years, as an index of the composition of this fluid, as well as a type of the mode in which an analytical inquiry should be conducted. Modern investigators have devoted themselves, with all the ardour and enthusiasm of a newly created or revived science, to the chemical examination of the urine, and hence modern literature is overcharged with works on the subject. We have here no lack of systematic inquiries, conducted from physiological, or pathological, points of view, or of individual analyses which have been undertaken with reference to some point of pure chemistry, or for purposes of special diagnosis. In the place of any such deficiency, we have so vast an accumulation of such labours, that one might be disposed to believe, judging by its bulk, that the study of the urine was the most complete portion of physiological chemistry. In how far such a belief is confirmed by fact, we leave the reader to determine from the following pages.

It is scarcely necessary to observe that the urine, when considered from a physiological point of view, must be regarded as a fluid secreted by the organism from definite organs—the kidneys—and containing certain soluble, nitrogenous, and saline substances, which have either become effete through the metamorphosis of animal matter, or have been conveyed into the animal body, but are injurious to the animal functions.

On examining normal human urine, we find that, when in a fresh state, it is of a lighter or deeper amber colour, and has a bitter, saline taste. When freshly passed, and while it retains the temperature of the body, it is perfectly clear and transparent, and has a peculiar, faintly aromatic odour. It is always somewhat heavier than water, although its density never rises above 1·03 (in the normal state). It distinctly reddens litmus paper, although not always with equal intensity. When the urine is kept in a clean vessel, it does not decompose so rapidly as has generally been supposed, especially when it contains a considerable amount of solid constituents. In urine, shortly after cooling, particularly if it be concentrated, and after it has remained for a long time in the bladder, as, for instance, in morning-urine, a light, cloudy film becomes formed, which gradually sinks to the bottom. The acid reaction gradually increases when the urine is kept for some time at a mean temperature, and yellowish red crystals, which are even discernible to the naked eye, are then deposited in the mucous sediment, and on the sides of the vessel. In this condition the urine may often continue unchanged for several weeks, without undergoing further decomposition; if, however, the urine be very dilute, and the temperature rises above the mean, a different process from that of acid fermentation is observed speedily to occur. The urine is then found to be covered with a thin, fatty shining, and frequently iridescent membrane, fragments of which gradually sink to the bottom. The mucous sediment is then interspersed with dirty yellowish white flakes, the urine acquires a pale colour, its reaction becomes alkaline, and it begins to develop a nauseous, ammoniacal odour. The reddish yellow crystals are replaced by white granules, which are intermixed with colourless, strongly refracting, prismatic crystals.

The urine of carnivorous mammalia differs little from that of man. It is perfectly clear, generally of a much lighter, almost straw-coloured hue, and strongly reddens litmus paper. The urine of herbivorous animals, on the contrary, is usually turbid, and in some cases even exhibits a decided sediment of a dirty yellow colour. It has a nauseous, sweetish odour, and an alkaline reaction.

The urine of birds and amphibia—animals in whom the ureters open into the rectum—is gelatinous, semi-fluid, and translucent, when freshly discharged; it rapidly dries in the air, and is then converted into white, cheese-like, crumbling masses.

The normal urine contains fewer *morphological constituents* than any other animal fluid, although the peculiarly formed *pavement epithelium* of the urinary passages, and more especially of the bladder, are never wholly absent. Virchow has drawn attention to the different forms of the epithelium of the bladder, which sometimes resembles three-toothed clamps, within which portions of the ordinarily shaped pavement epithelium are inclosed. The appearance of such cells in the urine is only of rare occurrence; they are found connected together, when the urine exhibits an abundant supply of epithelium, which had been peeled off within the urinary tubes; this is frequently the case after scarlatina, and less constantly after erysipelas.

The mucous sediment of normal urine is found, on a careful microscopical investigation, to contain well-formed *mucus-corpuscles,* having a simple, lenticular nucleus. These bodies occur in increased quantities even on slight irritations of the mucous membrane of the bladder, and, still more constantly, in vesical catarrh and pyelitis, when the urine often deposits a considerable, and apparently purulent sediment. In gonorrhœa, the mucus-corpuscles arising from the urethra are distinguished from those of the bladder and the remainder of the urinary tract by their greater size, and by their vitreous and but slightly granular appearance.

Among the different molecules of morbid urine which have been recognised by the aid of the microscope, special attention has been directed to the *tube-like, or cylindrical bodies* investigated by Nasse,* Henle,† and Simon.‡ On attempting to classify them by their texture, we find that they admit of being divided into three kinds: the first class embracing those tube-like formations, which appear to consist of the epithelial investment of the tubes of Bellini; they are tolerably regular cylinders, to which the small cells and nuclei appear to adhere in a somewhat honeycomb arrangement. These cylinders do not in general occur excepting in the desquamative stage of acute exan-

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* Correspondenzbl. rh. u. Westph. Aerzte. 1843, S. 121.

† Zeitschr. f. rat. Med. Bd. 1, S. 60 u. 68.

‡ Müller's Arch. 1843, S. 26.

themata, and at the commencement of every inflammatory irritation of the kidneys. The second class of these cylinders consists of fresh exudation, which is formed within the tubes of Bellini, whose shape it retains, and consists of cylindrically granular parts, inclosing blood-corpuscles and pus-corpuscles, and consisting apparently of fibrin; at all events they dissolve pretty readily in alkalies, while the inclosed corpuscles are partly destroyed and partly distributed in the fluid. As these are true croupous exudations, they necessarily appear in all the inflammatory renal affections which are usually included in the acute form of Bright's disease. There is, however, frequently a third form of these tubes, which occur in the shape of hollow cylinders with walls, which are so perfectly hyaline that they cannot easily be detected under the microscope, unless by modifying the light. They are frequently compressed together, or plaited as it were, and even in some cases coiled round their axes. They generally occur only scattered in the chronic forms of Bright's disease, as, for instance, in fully developed fatty degeneration of the kidneys. When treated with potash, they disappear, leaving only a fine, granular substance. An epithelial cell, or a rudiment of it, may often be observed in this species of cylinders, which I can scarcely regard as anything but the *membrana propria* of the urinary ducts. Acetic acid causes them to disappear, but I have been unable to discover by washing with water, or by neutralisation with acids, whether they have actually been dissolved, or have only swelled up, and have thus attained the same refracting power as the surrounding medium. They must not be confounded with the above described croupous cylinders of fibrin.

Spermatozoa are generally present in the urine after nocturnal emissions, or the act of coition, and they are also believed to occur in the somewhat rare affection of spermatorrhœa. They are not unfrequently found in the urine of typhous patients; although in these cases there may probably have been previous erection with a discharge of semen, yet in this disease, they would sometimes appear to have passed from the urethra into the bladder, since they have been found attached to its mucous membrane in the bodies of persons who have died of typhus.

Elongated mucus-plugs, which appear, when examined under the microscope, to consist of mucus-corpuscles arranged in rows, are frequently met with after gonorrhœa, and the so-called *goutte militaire.*

Blood-corpuscles are of frequent occurrence; and, as may be conjectured, they may originate from very different sources. They occur in small quantities in inflammations of the kidneys and urinary passages, but more especially in Bright's disease, in all the stages of which they have been found. If the urine be acid, the blood-cells remain for a long time without being decomposed, or at most become somewhat jagged; they are usually somewhat swollen, and approximate to the spherical form, being in general paler than in their ordinary condition, although still characterised by a strongly defined outline. The salts contained in the urine are probably the cause of their not assuming the nummular arrangement.

Large accumulations of *fibrin* only occur in the urine in acute inflammations of the kidneys or urinary ducts, and then always in association with blood-corpuscles.

When the urine is not perfectly fresh, it is found on examination frequently to contain certain organised matters, which may be classed among vegetable substances, or infusoria. These are gradually developed in the acid urine, and more especially in the mucous sediment, from which, as it would appear, there are formed certain microscopic *filamentous fungi*, which are very similar to the mykoderma cerevisiæ, differing only in being considerably smaller ($\frac{1}{280}$ to $\frac{1}{330}'''$), having a spherical rather than an oblong shape, and a distinct eccentric, round nucleus. They appear to be developed precisely in the same manner as the yeast-fungi; when the urine begins to lose its acid reaction, they may be observed upon the surface of the fluid, and probably contribute towards the formation of the membrane with which it is frequently found to be covered. The more complex vegetable organisms are not formed until the urine has begun to be alkaline; when we may observe numerous confervoid filaments, with or without spores, which often form a dense network, whose separate threads are commonly seen to extend over the whole field of view, even when examined with low powers.

Infusoria may always be detected in the urine after it has become alkaline: the form usually present is the ordinary filamentous or rod-like *vibrio* (*vibrio lineola?*), although moving molecular specks are also observed, which Höfle[*] regards as the *monas termo* of Ehrenberg.

We have already mentioned, at p. 136, that Heller seems on one occasion also to have found the *sarcina ventriculi* of Goodsir in the urine.[†]

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[*] Chem. u. Mikr. Nachträge, S. 159.

[†] [Heller has since recorded a second case. See Arch. f. Chim. u. Mikros New Ser. Bd. i., S. 30. A similar case has also been met with by Dr. Mackay. See Bennett's "Introduction to Clinical Medicine," 2nd ed., p. 96.—G. E. D.]

We now pass to the non-organic formations of chemical substances which occur in the urine, and which give rise to the urinary sediments when present in large quantities; amongst these the ordinary amorphous *urate of soda* occupies the principal place. We have already noticed this substance at length, at p. 214 of vol i., where we also referred to the occurrence of *urate of ammonia,* in the form of dark globular molecules studded with fine needles, in urine that has become alkaline.

The prismatic crystals of the *phosphate of ammonia and magnesia* occur only in neutral or alkaline urine; this substance was also noticed at p. 424 of vol. i.

The octohedral crystals of *oxalate of lime,* which are found in small quantities in the normal urine, and in greater abundance in certain morbid conditions, have also been described in vol. i., pp. 43—47.

The crystals of *cystine,* described in vol. i., p. 178, constitute a less frequent spontaneous sediment of morbid urine.

Urea occupies the first place amongst the *chemical constituents* of the urine, both because it exceeds in quantity all the other solid constituents of this fluid, and on account of the important part which this body plays amongst the *detritus* of the metamorphoses of animal matter, both in a physiological and in a chemical point of view. All these relations have already been fully considered in vol. i., pp. 153—168.

A similar observation may be made in reference to the *uric acid* present in the urine (vol. i., pp. 199—220.)

We have already stated in our description of the chemical and physiological relations of *hippuric acid* (see vol. i., pp. 188—199), that this acid must be regarded as a normal constituent of human urine.

Liebig's discovery that the nitrogenous and crystallizable bodies, known as *creatine* and *creatinine,* which are contained in the fluid of the flesh, also occur in the urine, induced us to enter into a full consideration of these substances in the first volume. (See pp. 134—142.)

We have already spoken in vol. i., p. 99, of the occasional presence of *lactic acid* and lactates.

We treated at pp. 318—321, vol. i., with all possible brevity, of the *extractive* and *colouring matters* of the urine; and as it would only lead to confusion, if we were to notice the numerous and fruitless observations which have been made on this subject, we will leave this question for the present, in the hope that it may speedily be elucidated by the scientific exposition of some able inquirer. There is, however, one substance concealed in these extractive matters, to which the attention of chemists has been specially drawn by Scharling.* This substance is contained in the ethereal extract of the urine, where it occurs mixed with pigment, with a fatty matter, and with volatile fatty acids. Unfortunately, however, all attempts to obtain this substance in a perfectly pure state for the purpose of investigation have hitherto failed. This body, to which Scharling gave the name of *oxide of omichmyl*, resembles resin, fuses in boiling water into a yellowish oil, and dissolves in alcohol, ether, and alkalies. It must for the present remain undetermined whether the acid reaction depends upon some acid associated with it, or whether it appertains to the oxide of omichmyl. When dry it smells like castoreum, but when moist it has a somewhat urinous odour, and when treated with oil of turpentine it developes a violet-like fragrance. It is decomposed by heat. On treating it with chlorine gas, Scharling obtained a substance whose composition was $= C_{14}H_5Cl\,O_4$, and therefore perfectly isomeric with chloride of salicyl. It must, however, still remain an open question, whether the oxide of omichmyl is actually precipitated, and the above described substance is a simple hydrogen-compound, $C_{14}H_6O_4$, of the chloride analysed by Scharling, this compound being isomeric with salicylous acid; for it might easily be the product of decomposition of a more complicated compound. Unfortunately the above described body was unfit for an elementary analysis, as it could not be exhibited in a perfectly pure state. This oxide of omichmyl did not yield the same reaction as the salicyl-compounds, when treated with nitrate of iron.

Mucous juice, as already mentioned, always occurs in the normal urine, although it is often present in very small quantities. It exhibits all the properties which are ascribed to the mucous juice generally (see p. 372).

We have already (see vol. i., p. 44) shown at length that *oxalate of lime* must be regarded as a normal constituent of the urine, in which it occurs in increased quantities during certain physiological and pathological conditions.

The *chlorides of sodium and potassium* occur in very variable quantities in the urine, as has been already stated (in vol. i., p. 430) It only remains for us to observe, that the quantities of the

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* Ann. d. Ch. u. Pharm. Bd. 42, S. 265.

alkaline chlorides are diminished in an extraordinary degree under certain pathological conditions; this being especially the case whenever copious transudations or exudations have been separated from the blood within a short period of time; but it is remarkable that this diminution is frequently only observable when we take into comparison the quantity of the alkaline chlorides discharged with the urine in twenty-four hours; this occurs, for instance, in acute dropsy, the acute form of Bright's disease, in copious diarrhœa, in cholera and typhus. On the other hand, the diminution of the metallic chlorides is frequently so considerable in inflammations accompanied with very copious exudations, that nitrate of silver will scarcely induce any decided turbidity in the urine when first discharged. This was observed by Heller,* first in pneumonia, and afterwards in other considerable inflammations. In the meanwhile this phenomenon is not constant, and may, perhaps, depend upon the amount of exudation that is formed. It is certain that this deficiency of the alkaline chlorides in the urine is of very short duration; indeed, I have never found it continue longer than three days. The quantity of the chloride of sodium rises, according to Heller, above the normal mean on the beginning of the resorption of the inflammatory exudation; but, although this may be possible, or even probable, it has certainly not as yet been proved; for, as we shall soon see, the method recommended by Heller does not afford the means of ascertaining the normal quantity of the chloride of sodium, or even of detecting a small excess above the average.

We have already spoken (in vol. i., p. 449) of the presence of *alkaline sulphates* in the urine; and it, therefore, only remains for us to state, that Heller has also attempted to investigate the fluctuations in the quantity of sulphates contained in morbid urine, by his method of applying baryta salts to urine which had been previously acidified. From these observations, he thinks he has found that the sulphates increase in the urine in inflammatory diseases proportionally to the degree of inflammation which is present.

I did not succeed in confirming Heller's statement in three successive series of experiments which I made on the urine discharged in the course of twenty-four hours by one pleuritic and two pneumonic patients. Relatively, the urine certainly contained more sulphates than in its normal state; that is to say, in 100 parts of

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* Arch. f. Chem. u. Mikros. Bd. 4, S. 516—526. [We may also refer the reader to a Memoir by Dr. Beale, "On the diminution of the chlorides in the Urine, or their absence from that fluid, in cases of Pneumonia," in the Transactions of the Med. Chir. Soc. for 1852, Vol. 35.—G. E. D.]

inflammatory urine (whose specific gravity was increased) there were more sulphates than in 100 parts of the normal (specifically lighter) fluid of the same patient after his perfect restoration. There were from 4·512 to 5·842 grammes of the sulphates of potash and soda (all the potash being calculated as combined with sulphuric acid) discharged by these patients during the twenty-four hours, whilst the urine discharged after recovery during the same period yielded from 4·974 to 6·582 grammes of the sulphates. Heller found the sulphates of the urine diminished in chlorosis, neuroses, chronic diseases of the kidneys, and in affections of the spinal cord; but, as the urine is generally very highly diluted in these diseases, we may conjecture that Heller, in estimating the volume of precipitated sulphate of baryta, may not have taken into account the large quantity of water in the urine. In one case of decided chlorosis, I found that 6·247 grammes of the sulphates of potash and soda were discharged in twenty-four hours.

The normal urine contains *acid phosphate of soda*, and not the basic phosphate, as asserted by Heller,—a fact that has been clearly shown by Liebig.* (See vol. i., p. 440.) This salt increases and diminishes, according to Heller, in nearly an equal ratio with the sulphates; Bence Jones,† however, once found them to be considerably diminished in a case of cerebral inflammation.

The *phosphates of lime* and *magnesia* occur in very various quantities in the normal urine; but where the food has been mixed, there are generally about 1·093 grammes of the earthy phosphates discharged by the urine in the twenty-four hours. The quantity of this salt in the urine depends in a great degree upon the nature and quantity of the food partaken of; that is to say, a much larger amount is secreted when the food is purely animal than when a vegetable diet is used. Thus, in my own case, while I continued for twelve days to live solely on animal food, I discharged, on an average, 3·562% of phosphates in the twenty-four hours. The quantity of phosphate of lime is often found to be considerably diminished in the urine of pregnant women, as Donné‡ has very correctly stated, and this is especially the case from the sixth to the eighth month of pregnancy; at the same time, the quantity of the lime is scarcely diminished. Here also the nature of the food may have exerted a special influence on the quantitative relations of the earthy phosphates in the urine, as may be seen from analyses

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* Ann. d. Ch. u. Pharm. Bd. 50, S. 161—196.

† Philos. Transactions for 1846, p. 449.

‡ Gaz. méd. de Paris, 1841. No. 22, p. 47.

of this secretion in its morbid state. In those acute diseases in which, on account of an antiphlogistic diet, only small quantities of animal food are taken, the secretion of the phosphates is very much diminished, as compared with that of the urea in the normal state. Heller, who has made important observations on the variations in the quantity of the phosphates, considers that they are increased in rheumatism and diseases of the ear, and diminished in acute and chronic spinal affections, neuroses, and in acute and chronic diseases of the kidneys.

If any evidence could be drawn from one observation, I might be induced to believe that there is an excessive secretion of the earthy phosphates by the urine in rachitis. A thoroughly rachitic child, aged four years, discharged by the urine, which was very acid and contained oxalate of lime, as much as 0·496 of a gramme of the phosphates in twenty-four hours; whilst another child of the same age, and who, like the first, had been fed principally upon milk, with some meat and white bread, secreted 0·345 of a gramme in the same period.

Iron is very commonly present in small quantities in the urine, although it is sometimes absent in this fluid in healthy persons. There has been much difference of opinion as to whether or not the urine in chlorosis contains iron; but this question might easily have been settled, if more practicable methods had been employed for detecting the iron. According to my own observations, iron occurs in the urine of chlorotic patients as well as in that of healthy persons, although it may in some cases be entirely absent; as the urine in chlorosis is generally poor in solid constituents, it is necessary to employ a large quantity of this secretion in order to detect its presence. It is, however, worthy of notice, that after the use of ferruginous preparations, whether employed in chlorosis or any other disease, iron may be detected in fresh urine, either directly by the ordinary reagents, or only in small quantities in the ash of the urinary residue. I have been unable to determine the relations which induce such an increased activity in the resorption of the iron as to enable larger quantities of it to pass into the urine.

A small quantity of *silica* may also be found in the urine, as was shown by Berzelius (see vol. i., p. 426).

The urine likewise holds in solution gases, namely, *carbonic acid* (Marchand*), with a little nitrogen. Both admit very readily of being exhibited by the method described at p. 330.

The quantity of *water* in the normal urine is so exceedingly

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* Journ. f. prakt. Ch. Bd. 49, S. 250.

different, even under purely physiological conditions, that no definite estimate can be made of it. The quantity of water which permeates through the kidneys is entirely independent of the quantity of solid urinary constituents which are simultaneously secreted; although, according to Becquerel's observations,* which I am able perfectly to confirm, large quantities of water may simultaneously carry off a large amount of solid constituents with the urine; that is to say, when large quantities of water have been drunk, more solid constituents are generally carried off by the urine in the twenty-four hours than when but little drink has been taken. But the quantity of water which passes off in the urine depends upon such various reasons, that the causes of its diminution and increase in this fluid cannot always be determined, even under purely physiological relations. These controlling causes are more especially the quantity of water drunk, or absorbed, in the bath, the nature of the stools, and the more or less copious transpiration, which again depends upon the external temperature, the degree of moisture of the atmosphere, bodily exercise, and many other internal and external causes.

Much obscurity long prevailed as to the cause of the *acid reaction* of the normal urine, which was originally referred to lactic and even to acetic acid; but this subject has at length been set at rest by Liebig, who has shown that the acidity of normal urine can alone depend upon acid phosphate of soda. Thus, for instance, when ordinary phosphate of soda (which, as is well known, yields an alkaline reaction) is dissolved in water, and the solution is gradually treated with uric acid, which exerts no reaction on vegetable colours, a fluid is obtained, which, on heating, reddens litmus paper, and on being cooled deposits a white crystalline powder, which exhibits under the microscope the most beautiful groups of prismatic crystals of urate of soda. Since so extremely weak an acid as uric acid can abstract from the phosphate of soda a portion of its base, we can hardly deny that stronger acids, such as hippuric, lactic, and sulphuric acids, may, immediately after their formation by the metamorphosis of animal matter, convert neutral phosphate of soda into an acid salt, in which form it then passes into the urine, together with the already formed sulphate, lactate, and hippurate of soda. If this mode of explanation be applied to the acidity of every species of urine, freshly discharged urine would not saturate a larger amount of base than would correspond with the quantity of phosphate of

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* Sémeiotique des Urines, &c. Paris, 1841.

soda which it contained. The observations necessary for determining this question are not, however, so easily conducted as one might at first sight suppose; for when the urine has been treated with so much alkali that its reaction is neither acid nor alkaline, there must obviously still remain the acid phosphate of soda in the solution; for the neutral phosphate of soda has an alkaline reaction, and, therefore, the acid salt cannot be neutralised whilst the urine continues to exhibit no reaction towards vegetable colours. On this account, I have endeavoured to determine the quantity of the free acid in the urine by the following method: I precipitate the urine with an excess of chloride of barium, and after boiling the precipitate with a very weak solution of sulphuric acid, determine the weight of the sulphate of baryta. I next digest equal quantities of urine with freshly precipitated carbonate of baryta until the acid reaction has entirely disappeared, and after acidifying the filtered fluid with a little acetic acid, precipitate by means of chloride of barium. This precipitate also is boiled in an extremely dilute solution of sulphuric acid, and then weighed; the quantity of the latter is far smaller than that of the sulphate of baryta first weighed, and this difference between the two weights gives the quantity of sulphate of baryta necessary to yield a sufficient amount of base to saturate the free acid contained in the urine. Hence we may easily calculate from the chemical equivalents the amount of the free acid or of the acid phosphate of soda. If this method did not lead us to calculate a larger quantity of acid phosphate of soda in the urine than it would appear from another mode of analysis there actually existed, the acid reaction would depend solely upon the acid phosphate. Although this was not unfrequently the case, I found still oftener that the opposite condition existed in healthy as well as in morbid urine; that is to say, a comparison of the baryta salts commonly yielded a higher number for the quantity of the acid phosphate of soda than was found by direct analysis to be present, and hence there must, in most cases, be some free organic acid present in addition to the acid phosphate of soda, or some other acid salt which reddens litmus paper. We must, however, beware of drawing too hasty a conclusion in reference to this subject, for the acidity of the urine often increases so rapidly after its discharge, owing to the formation of lactic or acetic acid, that the excess of free acid observed in the above mentioned experiments may perhaps be owing to the lactic acid formed after the urine has left the body. On the other hand, we frequently find such an excess of free acid in morbid urine, compared with the phosphate of soda, that this mode of explanation is no longer applicable. The acid reaction of the urine depends, therefore, in many cases, on the presence of hippuric and lactic acid no less than on that of the acid phosphate of soda. If, moreover, the latter substance alone were present in the urine, the phosphates of lime and magnesia could only be dissolved in it either as acid phosphates or by means of another free acid. But if, in this calculation of the free acid from the precipitated baryta salts, the earthy phosphates had been included in the weighing, the result always remained the same; or, in other words, there was more free acid than could be accounted for from all the acid phosphates of the urine. The water-extract of the urine commonly exhibits an acid reaction, notwithstanding repeated rinsing with alcohol, solely owing to its contained acid earthy phosphates, which must be present wherever lactic or hippuric acid constitutes the acidifying principle of the urine.

The spontaneous decomposition of the urine stands in the closest relation to the formation of its sediments, and even to the formation of the urinary concretions, as Scherer* has shown by several beautiful observations. We will next direct our attention to the almost normal sediment of the urine, which, as we have seen in vol. i., pp. 214—217, consists essentially of urate of soda, and commonly occurs under very different physiological and pathological relations. This sediment is often formed as soon as the freshly discharged urine cools, and hence we might be disposed to believe that its occurrence indicated nothing more than such an increase of the urate of soda that the latter could no longer be held in a state of solution in the urine at the ordinary temperature. This view is supported on the one hand by the fact, that such rapidly formed sediments of urate of soda are often completely dissolved on the addition of less concentrated urine, and on the other, by all these sediments becoming again dissolved as soon as the urine is heated to 50 or 60° C. But it hardly requires the aid of the thermometer to trace the connexion between the fall of the temperature and the deposition of a sediment, to convince ourselves that, in most cases, the turbidity and the formation of a sediment in the urine occur long after the temperature of the fluid has become identical with that of the surrounding atmosphere; thus a period of eight, ten, twelve, or even twenty-four hours, often intervenes

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* Ann. d. Ch. u. Pharm. Bd. 42, S. 171, and Untersuch. z. Pathol. 1843, S. 1—17.

before the deposition of the precipitate of urate of soda. The analysis of the urine shows, moreover, as Becquerel specially noticed, that a non-sedimentary urine very often contains a much larger quantity of urates than a sedimentary one. The separation of urate of soda must, therefore, depend upon some other cause than on the mere decrease of the temperature of the urine. The simplest induction leads us to assume that some alteration must occur in the urine when it is exposed to the atmosphere, which it does not experience within the bladder, and which is independent of a mere diminution of temperature. This alteration must, therefore, originate in some metamorphic process effected by the atmosphere in one or other of the constituents of the urine. The following facts induce us to regard the coloured extractive matter, or the extractive pigment of the urine as the substance which causes a large quantity of the urate of soda in the urine to remain in a state of solution, and which by its metamorphosis gives rise to the separation of a large portion of this urate. We know that this colouring extractive matter combines especially with the urates, whose properties it essentially modifies. I have elsewhere* shown that it is this extractive substance which hinders the urate of soda, when a warm solution is suffered to cool, from separating into the well-known groups of crystals; for if we add to a solution of urate of soda, which had deposited beautiful colourless bundles of crystals on cooling, some of the extractive matter of the urine which is soluble in alcohol, this salt loses its capacity for crystallization, and the same corpuscles are deposited in the cooling solution, which are generally found, although not in a crystalline form, to be separated from the urine, and which, moreover, occur in a smaller quantity, as may be seen by the naked eye, independently of weighing. Any one, moreover, who has collected on a filter this spontaneous urinary sediment, must have noticed that the metamorphosis of the pigment exerts a direct influence on the entire constitution of the urate of soda. On examining the deposit upon the filter, the bright red or even scarlet colour assumed by the sediment strikes the observer very forcibly; but on examining it more attentively, either through the microscope, or after we have attempted to dissolve it in hot water and to filter it, a number of the most beautiful crystals of uric acid will appear, of which not a trace can be discovered in the portion of the urine which was not filtered, and whose sediment, from not having been exposed to the action

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* Göschen's Jahresber. 1844. Bd. 2, S. 26.

of the air, exhibited no redness. All these appearances certainly indicate that the pigment of the urine, which, according to Duvernoy* and Scherer, participates in the separation of uric acid, may also contribute to the formation of the ordinary sediment of urate of soda. Even if we are not disposed to regard the extractive matter as a simple solvent, according to the above view, we might yet assume that the neutral urate of soda was dissolved in resh urine that was very rich in uric acid, whilst a little acid might be formed by this metamorphosis of the pigment, which might extract an equivalent of base from the simple urate of soda, and thus give rise to the formation of the bi-urate. (See vol. i., p. 203.) This view is corroborated, in the first place, by the fact that this ordinary sediment certainly does consist of the bi-urate of soda, and in the next, by the fact that in the above described experiment, in which the sediment had been collected on the filter, and it was then attempted to dissolve it in hot water, the filtered fluid did not exhibit an alkaline reaction, although a large portion of crystalline uric acid free from soda remained upon the filter. It requires, however, further experiments to elucidate this much neglected department of zoo-chemistry.

It must be observed, that Scherer has demonstrated, almost beyond a doubt, by means of several striking experiments, that the metamorphosis of the pigment exerts a great influence on the formation of the *sediments of uric acid.* We have already shown, in vol. i., p. 216, that, except perhaps in lithiasis, sediments composed of free uric acid never occur in freshly passed urine, nor can they be generated by the mere cooling of the urine. Hence I can only regard uric acid sediments as products of the decomposition of the urine after its removal from the animal organism. The different kinds of urine vary solely in respect to the rapidity with which any one kind of morbid, or normal, urine undergoes acid fermentation sooner than another, and thus gives rise to the formation of the insoluble sediments of uric acid. Scherer was the first who recognised and attentively followed this process of *acid urinary fermentation.* Every normal, non-sedimentary urine, when exposed to the ordinary atmospheric temperature, begins, after a longer or shorter period, to separate uric acid, and to exert a stronger reaction on litmus paper; we may, moreover, convince ourselves most strikingly of the increase of free acid in the urine by the volumetric method, which corresponds to the alkalimetric. Faintly alkaline urine, such as is passed after

* **Unters. über d. menschl. Urin. Stuttgart, 1835.**

vegetable food which is rich in alkalies, or after several doses of acetate or tartrate of potash, acquires, after a short time, an acid reaction, which increases so much under favourable conditions, that any turbidity, which may have arisen from the separation of earthy phosphates, disappears, and crystals of uric acid are separated. Scherer, and subsequently to him, many other observers, have noticed that jaundiced, brownish yellow, faintly acid urine becomes strongly acid, and that, in place of this colour, it assumes a green tint, owing to the peculiar action of the free acid on the bile-pigment.

The duration of the acid fermentation of the urine extends, according to Scherer, to four or five days, although, in a temperature of from 10 to 20° C., I have seen the acid of the urine increase for two or three weeks, and then often not disappear until after a period of six or eight weeks. Scherer explains this process on the supposition that the mucus of the bladder is a fermenting body, and that the extractive pigment is the substance metamorphosed into lactic acid. I have, however, frequently observed, as Liebig had previously done, that acetic acid is also present. Scherer's view derives support from the fact that the acid fermentation of the urine may be impeded, or interrupted, by most of the conditions which in other cases obstruct fermentation, as, for instance, by the addition of a little alcohol, by boiling the urine (when the formation of an acid is retarded for a prolonged period), and finally, by removing the mucus by filtration. The influence of the latter is also obvious, from the circumstance already mentioned at p. 398, that a species of fermentation-globules, or yeast-fungi, are generated in and from the mucus during the process of acid fermentation. I must again draw attention to the possibility that *oxalate of lime* may be formed, or, at all events, separated during this process of fermentation; at all events, the close connection between the separation of uric acid and the formation of this salt, seems to be proved by the fact that most samples of urine, whether sedimentary or non-sedimentary, exhibit no trace of the presence of oxalate of lime, when examined under the microscope, as long as they are fresh, although some of the known crystals of oxalate of lime may be detected as soon as the uric acid crystals are formed. Indeed, the abundance of such crystals in morbid urine is proportional to the rapidity with which acid fermentation is induced, and the consequent early deposition of free uric acid.

From the fifth day to the second or third week after the discharge of the urine, the free acid begins gradually to diminish;

confervæ and algæ are then observed, in addition to the filamentous fungi in the sediment and on the surface of the urine, when examined under the microscope. The urine finally becomes neutral, the yellow crystals of uric acid disappear, or in their place, we find the well-known crystals of phosphate of magnesia and ammonia, either in the form of large, colourless pyramidal prisms or in small radiated groups of needles or larger prisms. The urine becomes alkaline, acquires a most abominable odour, and is covered with whitish grey membranes, which swarm with innumerable vibriones and monads, in addition to vegetable products. The colour of the uric acid sediment is, with few exceptions, yellow, like its microscopical crystals, but when the deposit is *white*, it exhibits, not only the crystals of triple phosphate, infusoria and fungi, but also the brownish black, round clusters of urate of ammonia, studded on all sides with sharp needles. The urine effervesces strongly with acids; the fluid then scarcely exhibits any yellow colour, the pigment being consequently for the most part destroyed.

The *alkaline urinary fermentation* occurs, under certain partially unexplained relations, even before the completion of the acid fermentation, and sometimes even within the bladder. Normal urine passes more or less rapidly into the alkaline fermentation when the temperature exceeds 20° C.; this change is effected very readily when the urine has been kept in unclean vessels, and almost at once when mixed with urine which has become alkaline, even when the quantity added is so small as hardly to saturate the free acid of the fresh urine. We may, therefore, conclude that here, as in other kinds of fermentation, there is a special alkaline fermenting substance present, which, we believe with Scherer, can only be sought in the changed urinary mucus, and in the microscopical organisms contained in it. This mode of explanation is not only in accordance with the views which chemists now hold regarding the processes of fermentation, but it is likewise further confirmed by certain results of clinical experience. We have found that an alkaline urine which effervesces with acids is most constantly and distinctly observable in primary or secondary affections of the mucous membrane of the bladder. In the former case there either exists inveterate vesical catarrh or complete suppuration of the walls of the bladder in consequence of cancerous tumours or other secondary products; in these cases the secretion of mucus is abnormal, the mucous juice which is secreted in increased quantity, possessing none of the ordinary properties of urinary mucus, and being decomposed with extraordinary rapidity. In the latter case, the mucous membrane of the bladder, at most, suffers only indirectly; as, for instance, in affections of the spinal cord, accompanied with paralysis of the extremities and of the bladder; and if the vesical mucous membrane retain its perfect integrity, the mucus secreted from it cannot be thrown off on account of the deficient contractility of the bladder, but adheres to it, and begins to be decomposed to such a degree that it induces alkaline fermentation almost at once in the urine as it drops from the ureters, so that even in incontinence of urine, where the fluid had been retained only a short time in the bladder, it is both alkaline and ammoniacal when passed. Catarrh of the mucous membrane of the bladder is, however, only a secondary affection.

Scherer assumes from these facts, that the vesical mucous membrane may also acquire a condition within the bladder by which it predisposes the extractive matter to the formation of acid. This must undoubtedly be admitted to exist in the calculous diathesis, in which an acid urine is secreted with pre-formed crystals of uric acid; but the assumption of a mucus which is already modified before it leaves the bladder, does not appear to me to afford a satisfactory explanation in those frequent cases of febrile urine in which this secretion, when freshly discharged, exhibits a moderately acid reaction, and contains only urate of soda; for, independently of the circumstance that in those febrile or inflammatory affections in which we can scarcely assume the presence of any derangement of the mucous membrane of the bladder, or the existence of a mucus which has been modified within that organ, it frequently happens that one kind of freshly passed urine does not turn acid very quickly, nor is uric acid immediately separated from it, whilst urine which had been passed only two hours before may exhibit these properties in a very high degree. This phenomenon might be ascribed to the prolonged retention of a more concentrated urine, which might irritate the mucous membrane of the bladder, if the reverse were not occasionally observed, that is to say, if we did not sometimes find that one specimen of urine turns acid very readily and speedily, although another specimen, passed a couple of hours previously, may not exhibit the same properties for a prolonged period. We must here seek for the causes of the more rapid acidification of the urine in the constitution of the fluid secreted by the kidneys, that is to say, in the special condition of individual substances formed by the metamorphosis of matter during its modifications in fever, and perhaps more especially in the quantitative increase and the qualitative alterations of the urinary pigment.

Scherer has, moreover, endeavoured to show that these processes of fermentation, in so far as they occur within the bladder, contribute largely towards the *formation of calculi.* Thus, for instance, it depends solely upon the character of the vesical mucous and upon the nature of the fermentative process induced by it, whether the urinary concretion that is formed consist of uric acid, earthy phosphates, or urate of ammonia. The varying conditions of decomposition at different periods of the disease, that is to say, the gradual qualitative and quantitative change of the secretion of the morbidly affected mucous membrane, may afford an explanation of the formation of urinary calculi whose various layers have a different composition. Scherer thus seeks for one of the most important causes of lithiasis in a degeneration of the secretion of the vesical mucous membrane—a mode of explanation which derives support from the chemical investigations of urinary concretions as well as from medical experience. The majority of these urinary concretions contain a clot of mucus as a nucleus, whence it would appear that the mucus generally affords the first formative basis for the concretions; then, moreover, the inner layers of most calculi contain uric acid, whilst the outer ones contain earthy phosphates or urate of ammonia; a trace of uric acid, if nothing more, may always be detected in the nucleus of the concretion. Every uric acid concretion aids, by irritating the vesical mucous membrane, in increasing its own size by the deposition of phosphates or of the urates of ammonia and of lime; whilst it is obvious, from the formation of calculi, that at the commencement of their deposition mucus must almost always be present, and there must, at the same time, be a tendency to the separation of uric acid,—in short, an acid urinary fermentation. The uppermost layers of most urinary calculi show that, at the time of their deposition, an alkaline ferment was present, and that its action had already been established in the urine. All who have examined the constitution and formation of numerous urinary concretions, more especially of the larger ones, must be led almost involuntarily to the adoption of Scherer's view. Even the mulberry calculi, which undoubtedly contain a very large proportion of oxalate of lime, but probably never consist solely of this substance, furnish additional corroboration in support of this mode of explanation, for they always contain a large quantity of uric acid, and frequently constitute the nucleus of larger earthy concretions.

This admirable and simple mode of explanation, which harmonizes with the established views of the decomposition of organic substances, derives considerable support both from the chemical analysis of concretions as well as from medical experience, however widely it may deviate from the ordinary opinions of physicians who adhere to the idea of lactic, uric, and phosphatic diatheses. In the mean time it would be extremely difficult to prove that uric acid concretions owed their existence solely to a modification of the vesical mucus; for, as we have already observed, in speaking of sedimentary formations, there must be some controlling cause in the composition of the renal secretion, which in one case may facilitate and in another hinder the formation of concretions. There remain, probably, many other points which require to be investigated before we can explain all the phenomena relating to the formation of concretions, or hope to arrive at a scientific interpretation of the different forms of development of urinary calculi.

We will now proceed to the consideration of those urinary constituents which are *conveyed to the body from without*, and which, after remaining only a short time within it, *pass into the urine*, either wholly unchanged or in a slightly modified form. This subject, which is of the highest importance in the study of the metamorphosis of animal matter, was long since investigated by Wöhler,* and more recently by the same observer in conjunction with Frerichs.† Although it may appear somewhat illogical to notice the substances which, according to the experiments made in relation to this subject, do not pass into the urine, the present seems a fitting place to collect those facts which may serve as a positive basis for a theory of the formation of the urine, and aid in elucidating the internal mechanism of the zoo-chemical metamorphosis of matter.

It may be assumed as a general proposition, that such substances (not belonging to the nutrient matters) as are easily soluble in water, and exhibit no tendency to enter into insoluble combinations with the organic, or inorganic matters of the animal body, alone pass into the urine. On this account, most of the soluble alkaline salts, as nitrate of potash, borax, iodide of potassium, bromide of sodium, alkaline silicates, chlorates, carbonates, &c., are found unchanged in the urine. But in order that substances should pass unchanged into the urine, it is necessary that,

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* **Zeitschr. f. Physiol. Bd. 1, S. 305—328.**

† **Ann. d. Ch. u. Pharm. Bd. 65, S. 335—349.**

in addition to solubility, and the incapacity for entering into insoluble combinations, they should possess another character, namely, that of being already perfectly oxidised, or that of having no tendency to oxidation and decomposition generally. Thus, for instance, sulphide of potassium is a very readily soluble substance, which is not disposed to enter into insoluble compounds even with the matters within the animal body; but owing to the readiness with which it becomes oxidised, this substance does not pass into the urine unchanged, but in the form of sulphate of potash, unless too large a quantity have been introduced into the body. Many substances which enter into insoluble combinations with animal matters, as, for instance, with the albuminates, only pass into the urine when they have been conveyed into the organism in large quantities; hence Orfila found that the heavy metals, which are not in general separated by the kidneys,—namely, gold, silver, lead, bismuth, antimony, and arsenic,—might be detected in the urine, if administered in very large doses, but were commonly found to be present only in the liver and its secretion, and, consequently, also in the solid excrements, when they had been given in relatively small and frequently repeated doses.

Many organic substances undergo the same alterations in their passage through the animal organism which have been artificially produced by chemists; and this is especially the case with those organic matters which have been decomposed into different substances by the application of certain oxidising agents; there are even many soluble substances which become so perfectly oxidised in the blood, that neither they nor any of their products of decomposition can be recognised in the urine. Many others, on the contrary, which readily part with their oxygen, lose a portion of it in their passage through the animal body, and very probably in the *primæ viæ,* which causes them to appear in the urine in lower stages of oxidation.

We have already seen (in vol. i., p. 47) that after the use of drinks containing a large quantity of *carbonic acid,* the amount of the oxalate of lime in the urine is increased; but we must here observe, that we have found, from positive experiments, that the free carbonic acid of the urine is also very considerably increased by their use. After the use of champagne, the urine contains 53% of its volume of gas, and after that of Bavarian beer, 68%.

It has been observed both by Buchheim and myself, that Seltzer water did not produce the same effect as beer in the act of fermentation, or as sparkling wine, which may probably be owing to the circumstance noticed by Couerbe,* that when the pressure is removed from Seltzer water, it only retains one volume of gas, and probably loses a large portion of its acid by eructation after it has entered the stomach; whilst, on the contrary, champagne gives off only one half volume of its four volumes of condensed carbonic acid. It must be observed, however, that this transition of the carbonic acid from those highly carbonated drinks, or from alkaline bicarbonates, into the mass of the blood and the urine, is only very distinctly manifested when the substances in question are taken on an empty stomach. Buchheim has proved this to be the case, by repeated experiments on himself. A development of gas necessarily takes place as soon as food is introduced into the stomach, as we may readily comprehend from known physical and chemical grounds, and which is plainly manifested by eructations, and frequently also by flatulence, even enabling us in some cases to determine by percussion of the abdomen in what part the fluid containing the carbonic acid is in contact with the intestinal contents.

The *alkaline carbonates* obviously reappear, from what has been already stated, in the urine, although a portion of them must have been saturated by the acid juices of the stomach and intestines. It would be interesting to determine how much alkaline carbonate is necessary in order to induce the secretion of a neutral or faintly alkaline urine in man under definite conditions. Buchheim, who for some time instituted experiments of this nature on himself, found that even with reference to food and general dietetic relations, the quantity of alkali necessary for this purpose was extremely variable; this, however, is easily explained, when we consider how many causes there are which, in a greater or less degree, influence the acidity of the urine, and which are altogether beyond the control of the experimenter.

Iodine combines very rapidly with alkalies in the animal body, and then appears as iodide of potassium in the urine.

Soluble baryta salts, although they are so easily decomposed by sulphates, phosphates, and carbonates, yet, if given in sufficient doses, reappear, according to Wöhler, in the urine.

Ferridcyanide of potassium reappears in the urine as ferrocyanide of potassium.

Sulphocyanide of potassium, even when administered in small doses, may very soon be detected in the urine.

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* Journ. de Pharm. T. 26, p. 221.

It appears from the investigations of Wöhler, that most of the *organic acids* pass unchanged into the urine, when they are introduced into the system in a free state; he experimented with oxalic, citric, malic, tartaric, succinic, gallic, and salicylous acids.

Tannic acid is converted, in its passage through the animal organism, into gallic acid.

The observation made by Wöhler, that *benzoic acid* is separated from the animal body by the urine in the form of hippuric acid, has been confirmed by Ure,* Keller,† and many other observers.

The organ from whence the benzoic acid in this case obtains the elements of fumaramide (see vol. i., p. 198) cannot at present be decided with certainty; Ure believes that after the use of benzoic acid, the hippuric acid is increased in the urine at the expense of the uric acid, and that it consequently assimilates a nitrogenous group of atoms, which in its absence would have been applied to the formation of uric acid: hence he recommends physicians to employ benzoic acid against the uric acid diathesis. Unfortunately, however, Wöhler and Keller could not detect any diminution of the uric acid after the use of benzoic acid; and Booth and Boyé‡ arrived at the same conclusion. Garrod, on the other hand, believes that he has constantly found a diminution in the quantity of urea in the urine after the administration of benzoic acid; but neither Simon's investigations nor my own confirm this view. In four observations in which I examined the twenty-four hours' urine after the administration of large doses (two drachms) of benzoic acid, I failed in any case to detect a marked diminution of any of the nitrogenous constituents; experiments of this nature are, however, so difficult to execute, and the daily sum of the individual nitrogenous constituents is so fluctuating, that no conclusions should be drawn from such investigations; thus, for instance, it would be extremely rash to conclude, from the apparently negative result of the examination of the urine, that the benzoic acid abstracted nitrogenous matter from the substances designed for cell-formation.

If the close affinity that exists between benzoic and hippuric acids in some degree elucidates the production of the latter from the former in the metamorphosis of the animal tissues, the result obtained by Erdmann and Marchand§ is the more striking, namely,

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* Pharm. Trans. Vol. 1, No. 1.

† Ann. de Ch. u. Pharm. Bd. 43, S. 103.

‡ Medical Times, November, 1845.

§ Journ. f. pr. Ch. Bd. 35, S. 307—309.

that cinnamic acid, $C_{18}\ H_7\ O_3.\ HO$, in its passage through the animal organism assimilates nitrogenous matter, and escapes in the urine as hippuric acid.

There are various ways in which we may suppose that the conversion of cinnamic into hippuric acid may take place: it may either lose four atoms of carbon and two atoms of hydrogen, in order to be first converted into benzoic acid (for $C_{18}\ H_7\ O_3 - [4\ C + 2\ H] = C_{14}\ H_5\ O_3$), or by the assimilation of ammonia and the separation of water there is formed cinnamide ($C_{18}\ H_7\ O_3 + H_3\ N - HO = C_{18}\ H_9\ NO_2$), which has only to take up four atoms of oxygen in order to form water and hippuric acid ($C_{18}\ H_9\ NO_2 + 4\ O = 3\ HO + C_{18}\ H_8\ NO_5.\ HO$).

It is worthy of notice that *cuminic acid,* which is so closely allied to benzoic acid, does not resemble benzoic and cinnamic acids, in combining with nitrogenous matter within the animal organism, but passes unchanged into the urine; hence in its behaviour it resembles salicylous acid (hydride of salicyl) which is even more nearly allied to benzoic acid.

Wöhler and Frerichs have convinced themselves by experiments on several rabbits and dogs, that *uric acid,* whether introduced into the stomach or injected into the veins, is decomposed in the animal body in precisely the same manner as by peroxide of lead; the urine is at all events found to be far richer in urea and oxalate of lime after the administration of the acid.

We are indebted to Wöhler for one of the most important discoveries in physiological chemistry, namely, that the neutral salts formed by the combination of the alkalies with vegetable acids, are oxidised in the animal organism in precisely the same manner as if they were burned in oxygen gas: alkaline carbonates pass into the urine and render it alkaline; it consequently becomes turbid from the separation of earthy phosphates, and naturally effervesces with acids. That the conversion of the alkaline salts of the organic acids into carbonates takes place in the blood, might have been *a priori* concluded; but I have convinced myself, by the injection of an alkaline lactate into the jugular vein of dogs, that the change takes place with extraordinary rapidity, and that an alkaline carbonate very soon appears in the urine (see vol. i., p. 97). The same experiment has been made by others. It is, however, a singular circumstance, and one that requires further investigation, that in different persons, even under, apparently, precisely similar conditions, the period that elapses before the urine becomes alkaline, after the administration of these salts, is very various, and that in different cases very different quantities of these salts are necessary to render the urine alkaline. From the experiments of a young chemist, whose urine constantly became alkaline even after the use of a few baked plums, I was led to observe that in many persons who are living on a mixed diet, the urine becomes alkaline in two or three hours after swallowing half a scruple of acetate of soda, whilst in others who are living on a purely vegetable diet, two drachms of acetate of soda never succeeded in rendering the urine alkaline. From numerous experiments on healthy persons, and observations on patients who had taken alkaline acetates and tartrates, I could only deduce the following certain conclusions; when the salts in question exert a purgative action, the urine does not readily become alkaline; in fact, it seldom becomes alkaline at all under these circumstances: as might be expected, the urine of persons living upon animal food does not so readily become alkaline as that of persons living on vegetables and those on an antiphlogistic diet: if, however, the febrile affection be accompanied by a very acid urine, then it naturally follows that the urine is longer in becoming alkaline; hence two febrile patients might be taking the same doses of these salts, and the urine in one case might be alkaline and in the other it might remain distinctly acid. In one and the same person living on the same kind of food, the urine may become alkaline after a dose of these salts, if he remain quiet; but may retain its acid reaction after an equal dose, if he take strong bodily exercise. Hence we should be far from the truth if we believed that these points were thus cleared up; for a very small amount of observation at the bedside would suffice to convince us that we are far from being able to comprehend why, in special cases, the urine remains acid, or why it becomes alkaline. We must generally assume it as an undoubted fact, that the metamorphosis proceeding in the blood during the continuance of the morbid process tends, in a greater or less degree, to the formation of acid; and hence that in one of the cases, a smaller quantity of the vegetable salt is necessary to saturate the free acid of the urine than in the other case. The alkalinity of the urine during the use of vegetable diet appears, however, to be by no means solely dependent on the alkali contained in the organic salts of the food: for I have seen my own urine, which usually has a strong acid reaction, remain alkaline for eighteen hours after the use of food altogether devoid of nitrogen and alkalies, as, for instance, milk-sugar, starch, and fat. Magendie* injected a solution of starch into the jugular vein of a rabbit that fasted for three days, and whose urine was acid, clear, and rich in urea; the urine almost instantaneously underwent a complete change, becoming alkaline, turbid, and poor in urea. Bernard† injected a solution of grape-sugar into the veins of a dog and of a rabbit; the urine of both animals was thus rendered alkaline and turbid from the separation of earthy salts, while, under similar conditions, a solution of cane-sugar exerted no such action on the urine, but was carried off unchanged by that secretion. From these facts, we may undoubtedly conclude that the alkalinity of the urine of graminivorous animals does not solely depend upon the vegetable alkaline salts contained in the food. Bernard, moreover, found that the urine of dogs, which in the normal state is acid, becomes alkaline as soon as these animals are kept strictly upon vegetable food; and conversely, that the urine of rabbits, which under normal conditions is alkaline, becomes acid as soon as animal food has been introduced into the stomachs of these creatures, or a decoction of flesh is injected into their veins. From the experiments which Bernard instituted on herbivora, whose urine after the abstraction of all food was clear, of an amber-yellow colour, and strongly acid, it follows that the pure metamorphosis of tissue in the animal body, like a purely flesh diet, induces the secretion of a limpid, acid urine. Finally, Bernard believes that he has discovered that the pneumogastric nerves exert an influence on the reaction of the urine; thus, for instance, he saw that the alkaline urine of animals fed upon vegetables became acid after the section of both these nerves—a result whose accuracy I feel justified in doubting, having myself performed a similar experiment on a rabbit: rabbits are, however, by no means well adapted for such experiments; as far as my experience goes, these animals often secreting an acid urine without any apparent reason for so doing.

Quinine may be easily rediscovered in the urine after the use of moderate doses.

Urea, according to the experiments of Wöhler and Frerichs, passes unchanged into the urine.

Theine and *theobromine* cannot be rediscovered in the urine: since both these substances occasion intense excitement of the vascular and nervous systems, I am unable to decide whether the augmentation of the urea discharged in twenty-four hours, which I

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* Compt. rend. T. 23, P. 191.

† Ibid., pp. 536—537.

observed to occur, was dependent on the decomposition of these nitrogenous matters or upon the stimulus communicated to the entire organism.

Aniline, as it would appear from the experiments of Wöhler and Frerichs, does not re-appear in the urine.

No direct experiments have been made with other organic bases in reference to their transition into the urine.

Alloxantin appears, from the experiments of Wöhler and Frerichs, to be converted in the animal body into urea and other substances; they found neither the substance itself, nor alloxan, in the urine of persons who had taken five or six grains of it.

Thiosinnamine does not pass unchanged into the urine; in its place we find sulphocyanide of ammonium: hence it undergoes the same decomposition in the body as we can artificially produce by soda-lime. (W. and Fr.)

Allantoine does not pass into the urine, nor does it induce any augmentation of the oxalate of lime, as might have been expected; since it is decomposed artificially by alkalies into oxalate of ammonia (see vol. i., p. 174).

Amygdalin cannot be rediscovered with certainty in the urine. (W. and Fr.)

I could not detect the presence of *asparagin* in the urine.

Salicin undergoes the same decomposition in the animal organism that is induced by oxidizing agents. Salicylous acid* is found in the ethereal extract; it might be supposed that the salicin is decomposed in the animal body, in the same manner as by emulsin, into sugar and saligenin, and that it is only on the evaporation of the urine that the latter is converted by the free acid which is present into salicylous acid; since, however, no substance in the animal body acts upon amygdalin in the same manner as emulsin, it is by no means probable that salicin undergoes the last named mode of decomposition.

Phlorrhizin has not been rediscovered in the urine.

Volatile oil of bitter almonds (free from prussic acid) seems first to be converted into benzoic acid (without giving rise to any symptoms of poisoning), and then appears as hippuric acid in the urine. (W. and Fr.)

Quinone is decomposed in the animal organism. (W. and Fr.)

Benzoic ether causes an augmentation of the hippuric acid in the urine. (W. and Fr.)

According to Wöhler most pigments and many odorous

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* Handwörterb. der Physiol. Bd. 2, S. 15.

matters pass unchanged, or only slightly modified, into the urine; as, for instance, the colouring matters of indigo, madder, gamboge, rhubarb, logwood, red beet, and whortleberries, and the odorous constituents of valerian, garlic, asafœtida, castoreum, saffron, and turpentine. Wöhler could not rediscover the following substances in the urine:—Camphor, resins, empyreumatic oil, musk, alcohol, ether, cochineal, litmus, sap-green, or alcanna.

Another point worthy of notice is the *rapidity with which many substances pass through the animal organism.* We may generally assume that the rapidity with which a substance re-appears in the urine is directly proportional to its solubility, and inversely proportional to the amount of change which it undergoes in the animal organism. This rule, however, has many exceptions, amongst which we may especially mention iodide of potassium—a substance which is so easy of detection, even in extremely minute quantities; according to some observers it may be detected in the urine in from four to ten minutes after it has entered the mouth. I have only been able to observe this in a man in whom the posterior wall of the bladder, with the openings of the ureters, lay exposed; in other persons it often did not appear in the urine till after a period varying from three quarters of an hour to five hours, while, on the other hand, it was very soon to be detected in the saliva (see p. 23). After the ingestion of from two to three drachms of bicarbonate of potash, I have found, in experiments on several persons, that the urine became neutral in from thirty to forty-five minutes, and alkaline in the course of an hour. Lactate of soda taken to the extent of half an ounce, rendered normal urine alkaline in half an hour; on injecting similar quantities of the same salt into the jugular veins of dogs, their urine became strongly alkaline after five, or at the longest after twelve, minutes.

There is great diuresis in dogs after this operation if we provide them with plenty to drink; the loss of blood, even when small, seems to excite their thirst, while, on the other hand, the alkaline carbonate that is formed probably actually hastens the secretion of urine. Hence it is in general very easy to observe the time at which such urine becomes alkaline.

Erichson* observed the period of the transmission of soluble and colouring substances into the urine in a man with extroversion of the bladder—probably the same person who had been travelling about Germany; after administering forty grains of ferrocyanide of potassium, he saw it re-appear within two minutes in the urine:

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* Lond. Med. Gaz. June, 1845.

the ferrocyanide of potassium and other substances which were tried, appeared less rapidly in the urine when the experiments were made shortly after meals.

The period during which a foreign body remains in the animal organism is extremely various; here also it depends upon the solubility of the substance in question, and especially upon its chemical nature, whether a longer or a shorter time be required for its elimination. Substances of easy solubility are, as a general rule, rapidly removed from the body by the urine; thus I have seen the alkaline reaction of the urine disappear in as short a space as ten hours after a dose of two drachms of acetate of potash, while once after a dose of three drachms of bicarbonate of soda, it remained alkaline for three days. The idiosyncracy of each individual patient appears, however, to exert an influence on these relations. This is best observed in experimenting with iodide of potassium; in some persons no trace of this substance can be detected in the urine twenty-four hours after a dose of ten grains has been taken, while in others its presence may often be recognised after three days, both in the urine and also in the saliva. Substances which enter into insoluble chemical compounds with animal matters, are eliminated from the body only very slowly, and usually less through the urine than through the intestinal canal; metals, as is well known, are found after a very long time in the liver and in other parts.

We now proceed to the consideration of those *substances which usually only occur in morbid urine.*

Although an extremely large number of observations have been made regarding the occurrence of *albumen* in the urine, it has only been found to be constantly present in certain affections of the kidneys. Since we have possessed a more accurate knowledge of those forms of renal disorder which we know as Bright's disease, it has been established as a result of experience that albumen is always present in the urine in this affection, although its quantity may be so small that it may appear to be altogether absent. In the chronic form of Bright's disease the amount of albumen in the urine is often considerably diminished, if any acute or inflammatory disease be simultaneously present. The quantity of albumen in Bright's disease is, however, sometimes so considerable that, on heating, the whole fluid solidifies into a yellowish white coagulum. We cannot mention any other disease in which albuminuria is a constant symptom. Albumen is, however, very frequently present in the urine in all those diseases with which uræmia is associated, and particularly in scarlatina and other acute exanthemata, and most especially in cholera. Bright's granular degeneration of the kidneys is, however, very often present with uræmea, so that these diseases appear to owe their albuminous urine solely to the access of Bright's disease; there are, however, numerous cases, as for instance of scarlatina and erysipelas, in which albumen is only transitorily present in the urine for one or two days, and is accompanied by the epithelial cylinders, which have been already described. In these cases there is merely *simple renal catarrh*, in which, as in catarrhal affections of all other mucous membranes, there is desquamation of epithelium and a secretion of mucus.

In *dropsies*, at least in their more advanced stages, albumen is often found in the urine without the simultaneous existence of degeneration of the kidneys; in these cases there are two ways in which we can explain the manner in which this substance escapes from the renal capillaries: either the blood has already become so hydræmic that it not merely transudes through the capillaries of the peritoneum, of the subcutaneous cellular tissue, and of other organs, but also of the kidneys themselves, and that consequently some albumen is thus added to the substances which are ordinarily separated by the kidneys; or we may assume that those organic diseases of the thoracic or abdominal organs, which occasion a stasis of the circulation in the capillaries and veins of the abdomen, and thus give rise to copious transudations, also set up a similar condition in the capillaries and veins of the kidneys, by which an effusion of albumen into the urinary canals is induced. Meyer* has made some beautiful experiments on rabbits which support this latter view. On compressing with a ligature sometimes the renal vein on one side and sometimes the inferior vena cava, by which the increased hydrostatic pressure of the blood must dilate the renal capillaries, he always found albumen in the urine collected after the operation; and on tying the renal vein on one side he only found albumen in the urine that escaped from the exposed ureter of the side on which he operated, and here it was very abundant.

Organic diseases of the thoracic and abdominal organs sometimes occasion an escape of albumen though the kidneys, without, however, the simultaneous occurrence of any dropsical transudation; here the albuminuria probably only arises from the above mentioned causes.

If, in consequence of any affection of the urinary passages, *blood*, or true *pus*, should find its way into the urine, it is obvious that that fluid must then become albuminous.

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* Arch. f. phys. Heilk. Bd. 3, S. 116—119.

When albuminuria occurs in association with *hectic fevers, diabetes, diseases of the spinal cord, &c.*, this symptom is dependent either on the watery character of the blood, or, as is sometimes the case in diabetes, on an actual lesion of the kidneys.

The cases are by no means rare in which persons with only *slight fevers,* and unaffected by any other serious disorder, for a short time secrete a urine that is more or less albuminous (Becquerel,* C. Schmidt,† and others). Since we sometimes meet with cases in which the urine is albuminous when there is perfect health, and no cause can be assigned for its presence (Simon,‡ Canstatt,§ Becquerel,‖ and others), we are entitled to believe that some persons are specially predisposed to this affection, that is to say, that the facility with which the albumen escapes is dependent on a peculiarity of their organisation. We must here also notice the transitory occurrence of albumen in the urine during pregnancy (Rayer,¶ Becquerel,**). As the œdema of the lower extremities is closely allied to a varicose condition of the veins, so the overloading of the blood-vessels in the abdominal organs during pregnancy is probably a more efficient cause than any other of the transudation of the albumen into the kidneys.

We have already spoken of the occurrence of *fibrin* as an abnormal morphological constituent of the urine; and we remarked that it was always found in cases of hæmorrhage into the urinary passages. Urine is, however, occasionally observed in which only the intercellular fluid of the blood appears to have transuded; in some of these cases the fibrin becomes separated, after the emission of the urine, either as a gelatinous mass, or in granular clots or threads (Prout,†† Nasse,‡‡ Pickford,§§ Heinrich‖‖).

Casein has been particularly found in the so-called milky or chylous urine: I have frequently had occasion to remark in the preceding pages, how difficult it is to distinguish casein from basic albuminate of soda and other protein-bodies. I have never been able

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* Sémeiotique des urines, &c. P. 134.

† Charakteristik der Cholera. S. 117.

‡ Lehrb. d. med. Chem. Bd. 2, S. 382 [or English translation, Vol. 2, p. 184.]

§ Pathologie. 2 Aufl. Bd. 2, S. 182.

‖ Op. cit., p. 324.

¶ Maladies des Reins. T. 2, p. 579.

** Op. cit., p. 394.

†† On the Nature and Treatment of Stomach and Renal Diseases. 1848, p. 46.

‡‡ Unters. z. Physiol. u. Pathol. Bonn, 1835. S. 215.

§§ Arch. f. phys. Heilk. Bd. 6, S. 85.

‖‖ Rhein. Monatsschr. f. Aertze. Bd. 1, S. 24.

to detect true casein in urine; but in all the analyses of chylous urine, instituted by Chevallier,* Blondeau,† Rayer,‡ Bouchardat,§ Golding Bird,‖ and others, the evidence of the presence of casein is by no means established with scientific accuracy; for if it were, we must believe in a perfect metastasis of milk to the kidneys. It is, however, an unquestionable fact, that there do sometimes occur in the urine certain protein-bodies whose properties do not coincide with those of any known protein-compound, and whose modifications cannot be solely dependent on their admixture with the urinary secretion. Thus, for instance, Bence Jones¶ found a peculiar albuminous substance, together with the well-known tubular casts, in the urine of a man suffering from osteomalacia and from a renal disease; this substance was characterised by its solubility in boiling water; when precipitated by nitric acid it redissolved on the application of heat, but again separated on cooling; with acetic acid and ferrocyanide of potassium it behaved precisely as a protein-body, as also with concentrated hydrochloric acid, forming with it a brilliant purple solution; moreover, its elementary analysis showed that its composition was altogether analogous to that of the protein-bodies; it contained 1·1$\frac{0}{0}$ of sulphur, which could be very easily recognised on treating it with potash, &c. The urine contained 6·7$\frac{0}{0}$ of this substance, which cannot possibly be regarded as either albumen or casein, at all events until we are able by the addition of certain substances either to convert albumen or casein into this substance, or it into them; it presents too many points of difference to allow of our regarding it as a modification of any of the known protein-compounds.

Fat is comparatively rarely found in the urine, if we exclude the admixture of fatty matter that often arises from the external generative organs of women. In the older medical literature we often read of fatty urine, in which the fat collected as an iridescent film upon the surface; but in the great majority of cases these membranes must have consisted of the crusts of earthy phosphates and confervoid filaments, which have been already described, and not of fat; for these crusts are often singularly like a coating of

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* Journ. de Chim. méd. T. 4, p. 179.

† Ibid. Vol. 4, p. 41.

‡ L'Expérience. 1838. No. 12.

§ Journ. de Connaiss. méd. Août, 1843.

‖ Lond. Med. Gaz. Oct. 1843.

¶ Ann. d. Ch. u. Pharm. Bd. 67, S. 97—105 [and Philosophical Transactions for 1848, p. 55].

fat, which latter I have never observed on the urine. In more recent times Nauche* has regarded this membrane as a characteristic sign of pregnancy, and has instituted a number of experiments, which however only lead to a negative result. The *kyestein* is nothing else than the formation of crystals of triple phosphate, and fungoid and confervoid growths, which takes place when the urine becomes alkaline, as has been described in p. 410; but whether or not this membrane and the flocculent precipitate which is subsequently formed from it be actually a characteristic symptom of pregnancy, it cannot be denied that such a membrane, or, more correctly, the rapid alkalinity of the urine, is more frequent in pregnant women than in other cases; the urine of pregnant women is, as a general rule, very watery, and hence more readily undergoes alkaline fermentation; it further contains more mucous, protein-like substances than other urine, and this is a second reason why it more readily becomes alkaline and presents a tendency to the formation of this membrane. Hence Nauche's view is not altogether devoid of foundation; but every one must have observed that the urine of pregnant women, especially when they have been living chiefly on animal food, very often does not possess this property, and, on the other hand, that the limpid urine of hysterical and chlorotic women, as well as faintly acid and albuminous urine, may present precisely the same phenomena that have been regarded as peculiar to pregnancy.

It is in chylous and milky urine that the largest quantity of fat is found, where it occurs suspended in globules as in the chyle and milk. Unfortunately, very little is known regarding the forms of disease with which such urine is associated.

The occurrence of fat in albuminous urine is a symptom of more importance; it has been already mentioned (in vol. i., p. 254) that fat may be expected to be present in fatty degeneration of the kidneys; my own experiments on the urine in Bright's disease have not as yet confirmed this expectation; free fat-globules are, however, sometimes found in the urine, but it is never easy to decide whether they actually pertain to the urine, or, whether they are mere foreign admixtures; and the difficulty is increased by the very small quantity in which they always occur. In the latter stages of Bright's disease we sometimes, however, find individual tubes which appear to be filled with small globules or granules of fat, and present a striking resemblance to the *tubuli contorti* of fatty

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* Journ. de Chim. méd. 2 Sér. T. 5, p. 64.

kidneys. In such a case it would be quite possible to diagnose fatty degeneration of the kidneys from an examination of the urine.

By instituting a very careful examination, we may also sometimes find fat-globules in the urine in diseases which are accompanied with rapid emaciation; as, for instance, in certain diseases of the liver, and in those conditions with which hectic fever is associated.

We need hardly observe that *sugar* occurs in diabetic urine; it is, however, the quantity of sugar that is present which constitutes the characteristic sign of diabetes mellitus. It has been generally believed that sugar is also often found in urine which is not diabetic (Lersch*), but no very great weight should be attached to such an opinion, for the methods which have been employed for the discovery of sugar are open to many fallacies; even Trommer's test, when applied with every possible precaution, may give no decided reaction even when sugar is unquestionably present in urine; while conversely it may, in inexperienced hands, easily lead to the belief that sugar is present when in reality it is absent. It has been already mentioned (in vol. i., p. 289), that Prout and Budge have found sugar in the urine of gouty and dyspeptic persons, and that I detected it in the urine of a woman shortly after delivery; and I have the greater reason for believing that the results of these observers are correct, from the circumstance that I have very recently found sugar (by applying the method described in vol. i., p. 285) in the urine of a man with very acute gout.

Numerous cases have been recorded in which *abnormal pigments* have been found in the urine; the colour of the brick-dust sediments in febrile urine is unquestionably not dependent on the normal urine-pigment, although it may possibly arise from its oxidation; at all events, we very often see the ordinary urinary sediment (urate of soda) on the filter, of a deep brick-dust or scarlet colour; it has not been further examined; and at different times it has received the various names of *rosacic acid*, *uroerythrin*, and *purpuric acid*. Blue, green, violet, and black pigments are, upon the whole, of rare occurrence in the urine. We have already spoken (in vol. i., p. 319) of the pigments which Heller has exhibited from the urine; unfortunately, however, his experiments were so incomplete, that the very existence of such pigments as

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* Baier, medic. Correspondenzbl. 1846. S. 534.

uroxanthin and *urrhodin* is still doubtful; the one whose existence is most clearly established, and which admits of the most accurate examination, is the crystallisable *uroglaucin*, which has also been artificially obtained by Alois Martin* and by Scherer, by the action of nitric acid. This uroglaucin may possibly be contained in the blue, violet, and black urine of the earlier observers, and is probably identical with the pigment named *cyanurin*. Heller's assertion that the urine in Bright's disease and in cholera very often assumes a blue colour on the addition of very concentrated nitric acid, may be very easily put to the test; as far as my own experience goes, it is only when uræmic symptoms have manifested themselves that this peculiarity of the urine is generally observable.

The presence of the *biliary acids* in the urine is by no means so rare as has generally been supposed. Pettenkofer himself once detected them, by means of his own test, in the urine in a case of pneumonia; it is worthy of notice, that they are often present in only very small quantity, or are altogether absent, in well marked cases of icturus, even when the urine abounds in bile-pigment, while a urine which contains very little pigment is often found, on a careful investigation, to be comparatively rich in the biliary resinous acids. Cholic acid is, however, by no means invariably present in the urine in cases of pneumonia; indeed, it is comparatively seldom found in that disease. I have not been able to discover these substances in the urine in any other disorder, unless (as is often the case with pneumonia of the right side) there was a decided affection of the liver.

We have nothing to add to the observations already made (in vol. i., p. 316) regarding the occurrence of *bile-pigment* in the urine.

We must similarly refer our readers to vol. i., pp. 169 and 177, for all that need be stated regarding those comparatively rare substances, *xanthine* and *cystine*.

We have already noticed the pathological conditions under which *carbonate of ammonia* may occur in the urine.

Sulphuretted hydrogen, although in most cases formed in the same manner as carbonate of ammonia, has been occasionally found in the urine in cases of tuberculosis and rubeola by Chevallier,† Höfle‡, and Heller§.

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* Arch. f. Chem. u. Mikros. Bd. 4, S. 191—196.

† Journ. de Chim. méd. T. 1, p. 179.

‡ Medic. Ann. Bd. 11, S. 415.

§ Arch. f. Chem. u. Mikros. Bd. 3, S. 24.

Butyric acid, which was first detected in the urine by Berzelius,* is only rarely present in it either in health or disease. The occurrence of this acid does not seem to be associated with any definite form of disease; I have more frequently met with it in the urine of pregnant women than in that of non-pregnant women, or men.

Berzelius submitted to distillation urine that had been treated with sulphuric acid, saturated the acid distillate with baryta water, filtered, and obtained on evaporation a crystalline saline mass, which, on the addition of sulphuric acid, developed much butyric acid. On repeating the experiment, and submitting very large quantities of urine to such treatment, I never obtained more than traces of butyric acid; but on examining the urine of a woman who was not suckling (who was living on very low diet, and had little appetite), on the third, fourth, sixth, and ninth days after delivery, I obtained, by merely extracting the solid residue with ether, an acid fat which had the odour of butyric acid, and exhibited the ordinary properties of that substance: on then dissolving in water the residue that had been extracted with ether, adding sulphuric acid, and following the directions of Berzelius, I obtained a fresh quantity of butyric acid. This urine which contained butyric acid was always somewhat turbid and of a dirty yellow rather than an amber colour.

Ammoniacal salts, such as the hydrochlorate of ammonia, phosphate of soda and ammonia, and phosphate of magnesia and ammonia, do not occur in fresh urine, although their presence there has been often asserted. The experiments which prove the non-existence of ammonia in fresh urine have been described in p. 452 of the first volume. We have there also remarked that the efflorescence which is observable on evaporating a drop of urine under the microscope, depends neither upon hydrochlorate of ammonia, or phosphate of soda and ammonia. When, on the other hand, ammonia can be distinctly recognized in fresh urine after its evaporation, it must be the product of some decomposition. We have already alluded to the facility with which urinary pigment undergoes alteration, and thus hastens the decomposition of the urea. Any one, by repeating the following experiment which I devised, may readily convince himself that the presence of ammonia in even the most carefully evaporated urine affords no proof of its presence in the fresh secretion; for if we evaporate perfectly fresh urine in a retort at the lowest possible temperature, we always find ammonia in the distillate, while the concentrated urine that is left

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* Lehrb. d. Ch. Bd. 9, S. 424.

in the retort often reddens litmus paper more strongly than before. In this case the acid phosphate of soda exerts a decomposing action on the urea or on the pigment (probably on both), and there is formed phosphate of soda and ammonia, which, as is well known, evolves ammonia at a temperature of 100°, and again becomes converted into acid phosphate of soda; hence it exerts a continuous decomposing action on these nitrogenous matters during evaporation, and thus the urine may retain its acid reaction, while a large amount of an ammoniacal fluid passes over into the receiver. If we boil acid phosphate of soda with pure urea, or with the alcoholic extract, after freeing it from all bases and from ammonia by sulphuric acid, and saturating the sulphuric acid with potash or soda, we may readily satisfy ourselves of the correctness of this mode of explaining this singular phenomenon. On treating urine that has been concentrated by freezing with bichloride of platinum and alcohol, there is a precipitation of chloride of platinum and potassium, but no precipitation of platinum and ammonium; on adding caustic potash to such urine, the precipitate, when examined with the microscope, does not exhibit the well known star-like groups of laminæ of basic phosphate of ammonia and magnesia, but merely amorphous matter; and further, no ammonia can be detected in this precipitate by any chemical test.

It is universally known that ammoniacal salts occur in morbid, alkaline human urine; but we also sometimes find ammoniacal salts in the acid urine of patients, as I have convinced myself in examining the perfectly fresh acid urine of typhous patients. It is, however, extremely difficult to determine the quantity of ammonia with any moderate degree of accuracy, whether we apply bichloride of platinum according to Liebig's* method, or magnesian salts, as recommended by De Vry,† since urine of this nature has generally a great tendency to decomposition, and no conclusion can be deduced from a single specimen; for in the determination of the ammonia, it is necessary to employ the urine collected in a definite period. On this account also it is difficult to decide in what forms of disease we especially find acid urine to contain ammonia.

The following is De Vry's method of determining ammonia quantitatively in urine. Fresh urine is treated with bicarbonate of soda in order to remove the earths, is filtered, and sulphate of magnesia is then added to it; in consequence of the presence of phosphate

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* Ann. d. Ch. u. Pharm. Bd. 50, S. 195.

† Ibid. Vol. 59, p. 383.

of soda in the urine, the addition of the sulphate of magnesia causes a precipitation of phosphate of magnesia and ammonia, from which we must calculate the ammonia. There are, however, two points to be borne in mind, if we would wish to obtain accurate results by this method; the first is, that the bicarbonate of soda throws down some ammonia with the magnesia; and the second is, that it is possible that there may not be sufficient phosphate of soda in the urine to combine all the ammonia with the magnesia, and to precipitate them. Both these difficulties may, however, be readily overcome; the former, by determining the magnesia in the precipitate thrown down by the bicarbonate of soda, the latter, by the addition of an excess of phosphate of soda (Berzelius*).

The occurrence of *nitric acid*, which Prout† and Wurzer‡ believed that they had discovered in brickdust sediments, is very doubtful; for the methods of analysis which they employed might very easily deceive them.

In considering the *analytical methods* which have been employed, or suggested, for the examination of the urine, we find ourselves upon one of the most unpromising fields of inquiry within the whole domain of physiological chemistry. Our remarks as to the time and labour that have been lost in examining the analyses of the blood, apply with still greater force to most analyses of the urine. For these very analyses have been the means of throwing so much disrepute on the zoo-chemical investigations of true chemists, that they have been classed in the same catalogue with the much condemned analyses of old and modern drugs. We will only add a few remarks to what has been already stated in the first volume, in reference to the modes of discovering, and the methods of determining, individual constituents of the urine.

But if pathology has hitherto reaped only little advantage from analyses of the urine, the fault rests less with chemists than with physicians, who obviously can benefit little, or nothing, from even the best analyses of the urine, as long as they continue in error as to the actual results which may be obtained from such investigations. Till they learn to comprehend the questions they would submit to the chemist, they cannot obtain the desired reply from pathological chemistry. As long as the physician thinks he may employ chemical reagents as mere diagnostic instruments, like

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* Jahresber. Bd. 17, S. 628.

† Op. cit.

‡ Op. cit.

the stethoscope and the pleximeter, he will acquire but little information from a chemical investigation of the urine, which conducted on such principles will necessarily rank amongst the most slovenly experiments.

With respect to the *purely diagnostic investigation of the urine,* it may be observed that the application of the microscope, and some few chemical reagents will, in general, afford all the necessary means for answering the questions commonly demanded in chemical inquiry. If the urine be acid, the microscope may reveal, as we have already seen, mucus or pus-corpuscles (in the erroneously-termed chylous urine, such, for instance, as is almost constantly found to accompany pyelitis), epithelium, spermatozoa, casts from the tubes of Bellini, blood-corpuscles, &c., and in addition to these urate of soda, oxalate of lime and cystine ; if the urine be alkaline, a microscopical investigation will easily enable us to ascertain that the fluid contains only phosphate of magnesia and ammonia, urate of ammonia, and other morphological elements.

In order to distinguish *urate of soda* from uric acid in a sediment, by the aid of the microscope, the urine should not be heated, for this would dissolve the urate of soda, as has been mentioned in vol. i., p. 214.

If an apprehension be entertained of mistaking the molecular masses of urate of soda for other molecules under the microscope, a few drops of hydrochloric acid should be added to the object, when rhombic crystals of uric acid will be formed. (Acetic acid often acts imperfectly or very slowly.)

In order to avoid confounding certain crystalline forms of the *triple phosphate* with *oxalate of lime,* a little acetic acid should be added to the microscopical object, as directed in vol. i., p. 42.

The hexagonal tablets of *cystine* may readily be, and probably often are, confounded with the analogous forms of *uric acid.* They may, however, easily be distinguished under the microscope, on the addition of acids ; since the crystals of uric acid, which are generally yellow in colour, are insoluble in them, whilst the crystals of cystine (which are generally colourless) very rapidly dissolve in them. We have already spoken in vol. i., p. 178 of the chemical means of recognising cystine.

Other substances, such as *urea, hippuric acid, uric acid* (when it is not contained in the sediment), *albumen, sugar, the biliary acids, and bile pigment,* can only be chemically recognised in the urine by the methods which we have already considered in the first volume.

We have already noticed the mode of detecting *butyric acid,* certain abnormal *pigments,* and *ammonia.*

With a view of determining the average quantitative relations of certain inorganic constituents, the same reagents are generally employed which are used in their qualitative analysis; thus, for instance, in order to detect an excess or a deficiency of hydrochloric, phosphoric, and sulphuric acids, and lime, in the urine, nitrate of silver, acetate of lead, chloride of barium, and oxalate of ammonia are usually directly added to separate specimens of urine —a mode of proceeding which can scarcely be justified, even in a medico-diagnostic investigation. Care should at all events be taken to bring the different samples of urine which are to be compared with the normal secretion to the same degree of density by concentration, since it is by this method only that a comparison can be made between the volumes of the precipitates. Such a method would, however, consume more time than observers are willing to expend on the inquiry, although it must be obvious that such a comparison of the volumes of the precipitates cannot in itself lay claim to the slightest degree of accuracy. How many substances may not be contained in the precipitated metallic salts, even where nitric acid has been most carefully employed for the recognition of the chloride of silver or the sulphate of baryta? May not numerous organic substances be precipitated by the metals from the urine, more especially when it is in a morbid condition? How is it possible to decide regarding the density of the urine from its colour, or in this manner to determine the excess, or diminution, of these substances? Physicians should be cautious, lest they may be led into new errors by these superficial chemical tests, when they have only just liberated themselves, by physical and anatomical investigations, from older misconceptions. It would, however, be going too far, were we to attempt wholly to avoid these misapplied methods, in entering upon a scientific examination of the urine. Thus, for instance, in attempting to ascertain the increase, or diminution, of the phosphates in any disease, we might, after collecting the twenty-four hours' urine, and keeping it as cool as possible, add ammonia in order to remove the earths and the greater part of the uric acid, and then treat the filtered fluid with sulphate of magnesia. The first precipitate after exposure to a red heat would show the amount of the earthy phosphates, and from the second we could calculate the phosphate of soda. If we wish to ascertain the quantity of lime separated with the urine in a certain time, it would be sufficient to precipitate the filtered urine with oxalate of ammonia, (provided the urine be acid,) and after the oxalate of lime has been washed according to the usual methods of analytical chemistry, to expose it to a red heat, weigh it, and thus calculate the quantity of the lime. If we precipitate acidified urine with a baryta salt, we may approximately determine the quantity of sulphuric acid; but if we follow all the prescribed rules, we shall, after exposure to a red heat, obtain a carbonaceous sulphate of baryta, which after the combustion of the carbon will exhibit an alkaline reaction or develop bubbles of air, when treated with acid. A similar remark may be made in reference to the determination of the chlorine in the urine by direct precipitation.

The method of determining the potash in the urine by bichloride of platinum would, for reasons which remain to be explained, be almost equally devoid of exactness with the modes of determination already referred to.

It must be observed in reference to the qualitative investigation of the urine, that it is very instructive to allow this fluid to stand for a prolonged period, and to examine it from time to time with the microscope, since the nature of the physical alterations, the rapidity with which they occur, and the changes observed in the reaction on vegetable colours, yield, as we have already seen under the head of Urinary Fermentation, considerable information as to the presence of such ingredients or characters of the urine as could not be chemically detected.

More importance has been attached to the determination of the *specific gravity* of the urine than it actually possesses in a scientific point of view, or than it merits from the methods employed in determining it. In fact, the determination of the specific gravity of the urine is of less importance than that of any other animal fluid. We may regard it almost as a law, that the blood, and most other animal fluids, have always a tendency to maintain a definite specific gravity, which is necessary for the fulfilment of their functions. The fluctuations in the specific gravity of these fluids are, therefore, very inconsiderable, and hence it is the more important to notice great variations in them. The case is altogether different in respect to the urine, whose concentration is almost invariably changing; indeed, it seems to be the special function of the kidneys to maintain the other animal juices in their normal state of admixture and in their proper degree of concentration; at one time there being an excess of salts carried off with the *detritus* arising from the metamorphosis of tissue, at other times, more or less water. We have already shown what numerous and different external and internal conditions control the quantity of water which passes through the kidneys, and we can therefore derive but little instruction from a knowledge of the specific gravity of the urine, while we remain in ignorance of the conditions which exist in individual cases.

It may be asked, however, will not the specific gravity of the urine aid us at the bedside in arriving at important conclusions regarding the course of the morbid process, or even in recognising the disease? But, notwithstanding the use of the highly vaunted *urinometer,* which has been constructed in various forms and according to different principles, we do not find that the more accurate determination of the specific gravity of the urine has thrown any great light upon the morbid processes in question. Nor indeed was this to be expected, for it is far more difficult to draw any scientific conclusions from the density of the renal secretion in the diseased organism than in health. But may it not be objected, that the specific gravity of the urine may aid in the diagnosis of diabetes mellitus? This very questions shows that the importance of determining the density is ideal rather than real, for the specific gravity of diabetic urine, even when the disease has been diagnosed, is frequently not greater than that of other urine; even when diabetes is fully established, this is very frequently the case; so that the colour and reaction of the urine, and the quantity daily discharged, must be taken into account in forming a diagnosis from the urine alone. But surely it would be much better at once to apply one of the simple tests; for sugar, if found to be present, would have a higher diagnostic significance than all the other characters together. Why should a bad method be employed when a good one is at our disposal? The urea diathesis assumed to exist by English physicians, may perhaps be diagnosed from the specific gravity of the urine; as yet, however, this disease has not, so far as we know, been observed on the continent, and, indeed, we almost doubt if it ever will be, for a disease which consists of a mere metamorphosis of all the tissues into urea, without any special anatomically demonstrable organic lesion, is not credible on physiological grounds. How rapidly this supposed chronic affection would run its course, if such masses of urea passing daily through the urine were the *detritus* of the tissues, and not, as is probably the case, merely the result of a good digestion of large quantities of animal substances!

The specific gravity of the urine has never been determined on account of its absolute value, but always solely with the view of determining the quantity of solid constituents and water contained in this fluid. It was supposed that the residue of the urine might readily be determined from its specific gravity, and for this purpose Fz. Simon,* Becquerel,† and G. Bird‡, have attempted to establish formulæ from which, when the specific gravity was given, the solid residue of the urine might be determined. The complete inapplicability of such formulæ, which I have shown by my own experiments,§ has recently been most completely demonstrated in a large number of investigations made by Chambert‖ on the urine of healthy persons. These experiments prove that there does not even exist any definite proportion between the quantity of salts in the urine and its density, and much less that any such connection exists between the organic matters and the density of the fluid. A comparison of the numbers yielded by the formulæ of these three observers will suffice to show the remarkable differences in the results. These differences are clearly exhibited by the following simple illustrations; thus, for the urine whose specific gravity is 1·010, Becquerel gives 1·650%, Simon 1·927%, and Bird 2·327%; for a specific gravity of 1·020, the first gives only 3·300%, the second 4·109%, and the last 4·659%, &c. If this enormous difference in the results depend upon the different methods adopted by the several observers for the determination of the specific gravity as well as of the solid residue, it is evident from Becquerel's tables, in which the specific gravity is only increased about $\frac{1}{1000}$th part and the urinary residue about 0·165%, that a progression which is so much at variance with all the laws of physics cannot be correct. It would be necessary to expound the principles of physics, were we to attempt, in the present place, to explain why two or three kinds of urine may have the same specific gravity, and yet differ in the quantities of their solid constituents, and why, conversely, samples of urine which contain similar quantities of solid constituents, might yet differ so considerably in density. In order, however, fully to show the impracticability of this method, we need only refer to the remarks made at p. 4, in reference to the determination of the specific gravity as a means of controlling the chemical analysis. It is obvious, from Schmidt's positive investigations, that a definite

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* Beiträge z. med. Ch. u. Mikrosk. Bd. 1, S. 77 u. 143.

† Semeiotique des urines, &c. P. 33.

‡ London Medical Gazette. New Ser. Vol. 1, p. 138.

§ Schmidt's Jahrb. Bd. 47, S. 5.

‖ Recueil des Mémoires de méd. et pharm. milit. T. 58, p. 358.

progression in the specific gravity which may be expressed numerically, cannot correspond with that of the increase of the solid constituents; and that in the analysis of the urine, Schmidt's mode of determining the specific gravity, *as a volumetric check* on the chemical determinations, possesses only a fictitious accuracy. The reasons of this uncertainty consist partly in our ignorance of the coefficient of condensation of many of the constituents of the urine, which are present in very variable quantities, and partly on the utter impossibility of determining the quantity of some of the substances contained in the urine, even with a moderate degree of accuracy.

Although we regard it as entirely out of place in a work on physiological chemistry, to enter more fully into the methods of determining densities, or to pass an opinion upon their value, since these are subjects which should be learnt from physics, or at all events from practical chemistry, we cannot forbear making a few remarks, which may prove serviceable to those who have been unable to form any opinion regarding the numerous determinations of densities with which pathologico-chemical literature is overburdened. The ordinary means employed for the determination of the specific gravity of animal fluids are, the areometer, the hydrostatic balance, and the direct weighing of equally large volumes of distilled water and of the fluid in question. We need hardly repeat an observation which we have already made more than once, that the areometer gives only approximately correct results, even when it has been graduated for a definite temperature, and is in other respects well made. It would, however, be wholly at variance with the principles of areometry, if we were to expect to arrive at even a tolerably accurate result, if we applied the areometer to fluids containing any solid particles in suspension. Even if such approximate determinations may suffice in the case of analyses of the urine, they should be discarded in all other animal fluids; for if the specific gravity is to be anything beyond a mere appendage to the analysis, its approximate determination will simply furnish a means of error. Our remarks naturally apply to all the other methods in use for determining the densities of fluids, and even with greater force, in so far as they justify us in expecting more accurate results than those which can be furnished by the areometer.

Among the different areometers, there is only one which deserves any special notice; but this instrument, which is constructed by Alexander,* of Münich, yields, according to my experience, much more accurate results than one might be disposed to expect, *a priori*, from its construction. It is arranged in the following manner:—Two parallel graduated glass tubes, both open at one end, and communicating with each other at their other ends, at which is a small syringe, are introduced, the one into water, and the other into the liquid to be examined. The air in the tubes is now slightly rarefied by means of the syringe, when, by comparing the elevation of the water and of the other liquid in the tubes, the ratio of the specific gravities is given. This is the best of all the instruments for rapidly determining the density, as the influences of the temperature and of atmospheric pressure are here almost eliminated.

The *hydrostatic balance with a glass sinking-ball* generally yields more accurate results than the areometer; but yet, notwithstanding every precaution, it does not admit of the exactness presented by the direct weighing of volumes. The defects in this method depend principally upon the irremediable loss of a portion of the water of the animal fluid by evaporation, and more especially upon the circumstance that the balance gives a much less accurate result when the glass ball is weighed in water or in an animal fluid than when it is weighed in the air; and on this account fluids that are at all viscid, such as blood-serum, should not be treated by this method: defibrinated blood cannot be examined in this manner, for we often find that even the addition of one or two centigrammes does not affect the beam of the balance. Even if the unavoidable adhesion of vesicles of air to the glass did not render this mode of determination unsuitable for the blood, its employment in the case of a fluid in which solid particles are irregularly distributed, appears, from well-known physical grounds, to be wholly irrational.

The ordinary method of determining the specific gravity by the *direct weighing of equal volumes* in glass flasks is the best, but its value may unfortunately be very considerably diminished if it be not conducted with a care and attention which many medical chemists scarcely seem to think necessary, excepting in the case of elementary analyses. It is not sufficient in this method to weigh the empty and carefully dried flask, to determine its weight when filled with water, and finally with the fluid to be examined, for several calculations will be required to make the necessary corrections, on account of differences in the thermometric and barometric

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* Polytechn. Centralb. 1847. Heft. 6, S. 361.

relations. It must further be borne in mind that the weighing is not conducted in a vacuum, and that the specific gravity alone possesses any value when it has been reduced for a vacuum. This is easily effected when the specific gravity of the glass and the coefficients of expansion of the air and water are known; and the calculation may be very considerably shortened by the use of logarithms, or of a couple of algebraic equations.*

But in how few of the numerous determinations of the density of animal fluids has it been thought necessary to employ all these precautions! No one, however, who compares the results obtained with and without these corrections can deny their necessity. Then, moreover, we very rarely find the mode of determination indicated in the notice of the specific gravity, although the knowledge of the method employed is quite as important here as in the case of the numerical results of the analysis. How can we place entire confidence in the technical mode of conducting such a determination, when this essential part of the calculation of the specific gravity has been neglected? We can hardly expect that an experimentalist who neglects to attend to the influences of temperature and the degree of expansion of the different media employed in these measurements, should regard all the other necessary precautions; amongst which, we may enumerate the following as points worthy of attention. In every experiment for the determination of volume, we should use freshly boiled distilled water; the glass should be held and dried with some non-conducting substance, and care should be taken to avoid all contact with the heated or perspiring hands; all vesicles of air should be excluded as far as possible, and the glass cover or plate should be moistened before it is placed upon the flat surface, in order to remove any adhering air; and the flask should be dried with some cleaner substance than ordinary linen or strips of paper, which may give rise to great inaccuracy.

The practice of drying the flask by means of a wire wrapped in linen or paper, is not only laborious and tedious, but may, at the same time, give rise to slight errors; on which account, it is better to place the flask over sulphuric acid in a vacuum, which accomplishes the proposed purpose very rapidly and effectually; or, after the flask has been placed in the sand-bath, the air may be suffered to pass through it, as in smoking, by means of a

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* We would refer those who may be ignorant of the mode of constructing the necessary formulæ, to any of our best Manuals of Physics, and especially to Berzelius's Lehrb. d. Ch. 3rd Ed., Vol. 10, p. 285, and to C. Schmidt's Entwurf einer Untersuchungens methode thierischer Säfte,

tube running along the bottom of the vessel. By these methods, which are familiar to all chemists, the faintest breath may be observed upon the exterior or interior of the glass. We simply refer to this well-known operation, in order to show those less familiar with this apparently simple method, how much care and attention are required for the mere determination of the specific gravity of a fluid.

Having already offered these remarks on the methods of determining the specific gravity, it may not appear superfluous to observe that we have been induced to adopt this course on two different methodological grounds. The first, which has already been noticed, refers to the necessity for the utmost accuracy where we are desirous of imparting any scientific value to our determinations of density as a controlling test of the chemical analysis, and as a means of comparison with the specific heat and the refractive and polarizing powers; since, without such precaution, the scientific object of the inquiry could never be attained. The method alone is not all that ought to be considered, since the mode of its application is of even greater importance; for whilst one person may obtain very incorrect results in weighing with the most accurate balance, another may contrive to arrive at the best determinations by means of an inferior balance, provided the weights are accurate. Thus, too, the second reason which has led us into some diffuseness, is obvious from our previous observations, and consists in this: that we should regard all average estimates of density which are prosecuted simply by way of appendage to the chemical analysis, or for the purpose of roughly determining the quantity of water in a fluid, as entirely superfluous, and a mere waste of time and labour which might have been expended upon some of the numerous questions of science which still require elucidation.

In passing to the consideration of the *quantitative analysis* of the urine, we need only observe generally, that in all investigations of the urine, in which the quantitative relation of the secreted urinary constituents is to be ascertained, the collective fluid which has been passed within a definite period (as, for instance, twenty-four hours) should be selected for analysis, and its composition compared with that of other normal or morbid urine which has been passed in the same period of time; or in case this method is not practicable, or is otherwise unsuited to the object of the investigation, the quantity of water should be wholly disregarded, and the proportions of solid constituents to one another should be made the object of investigation (that is to say, the constituents should be calculated for 100 parts of solid residue). So much has already been said in reference to the necessity of this point in a rationa investigation of the urine, as insisted upon in Becquerel's and my own observations,* that it would be alike uninteresting and superfluous to revert to the reasons which led us to establish this rule, more especially as it must be obvious from all that has been, and still remains to be, mentioned concerning the urine. It may, however, seem as if we were too strenuously insisting upon this very important point; for this rule by no means entirely precludes the analysis of any other urine besides that which has been collected in twenty-four hours. For, independently of the fact that the analysis of the entire quantity of urine discharged from the bladder at one time, is not only admissible, but even highly desirable, when considered in a scientific point of view, we may derive accurately scientific and purely physiological results by adopting a method I have elsewhere recommended, of comparing together the different solid constituents in the urine, without restricting the examination to the twenty-four hours' urine. The comparison of the numbers representing the solid constituents frequently gives very unexpected results, which cannot be obtained from a mere comparison of the complete analysis of the twenty-four hours' urine, or of any other urine. By way of illustration, we will simply refer to our remarks at p. 95, in which we showed that we had been enabled, by a comparison of the solid constituents of hepatic venous blood with those of portal blood, to arrive at several conclusions which could not have been obtained independently of this mode of calculation, but which are very important, and throw considerable light on the metamorphoses effected in the liver, the physiological import of the hepatic function, and the rejuvenescence of the blood. This is even more essential in respect to the investigation of the urine, since water in general plays a far less important part, or, at all events, does not stand in so definite a relation to the solid constituents here as in other animal fluids,—a remark which applies equally to daily urine and to any individual specimen. Indeed it would be wholly illogical to insist that analyses should be rigorously limited to the twenty-four hours' urine, since such a method could not fail to lead to errors and misapprehensions. We need hardly remark, that in acute diseases the character and composition of the urine may change very considerably in the course of twenty-four hours; and this is not only the

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* Journ. f. pr. Ch. Bd. 25, S. 1-21, and Bd. 27, S. 257.

case in typhus, measles, &c., but sometimes also in inflammations running their ordinary course. Thus it not unfrequently happens in pneumonia, that a urine is passed in the morning, which either already exhibits an alkaline reaction, or becomes alkaline in a very short time, whilst the urine discharged three or four hours later may have an acid reaction, and exhibit an increase of acidity on standing. Now, when such different kinds of urine are mixed, we can hardly be said to be conducting a very strict, or even rational, method of investigation.

In conducting an analysis of the urine, special attention must be devoted to its evaporation and the drying of its residue; and here again we encounter other difficulties, which differ from those presented by similar modes of investigation, as, for instance, in evaporating and drying milk. I have convinced myself by direct experiments* that, in *evaporating* the urine, its decomposition will be directly proportional to the duration of the evaporation; and I have already drawn attention to the fact that the urine always develops ammonia during its evaporation, although it may retain its acid reaction. It is, therefore, very important to let this evaporation be effected as rapidly as possible, when it is unavoidably necessary to do so by heat; and this observation is especially applicable when the collective twenty-four hours' urine is evaporated, since in this case the urine is rendered more susceptible of decomposition from prolonged standing. Slow evaporation has, however, the effect of causing the urine to become decomposed with extraordinary rapidity, as we may see from the fact that urine which has been thus collected and mixed together will, in four out of five cases, contain no hippuric, but only benzoic acid. The urine always becomes slightly decomposed when evaporated by heat, in whatever manner this may have been accomplished; but the following method is, I think, the best adapted to hinder, as much as possible, this decomposition. The urine should be introduced into a wide tubular retort, and whilst the evaporation is proceeding on a sand-bath near the boiling point, atmospheric air, or hydrogen gas, should be continually passed over the evaporating surface. The distillate will then always be ammoniacal, although not to such a degree as if the evaporation were accomplished without the employment of a current of air. The quantitative determination of the solid residue cannot, however, be obtained by this method, which simply serves for the preparation of the extract from which

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* Op. cit.

the urea and the other constituents of the urine may be quantitatively determined.

I regard the following as the only correct method of ascertaining the quantity of the solid residue: small quantities of the fluid (see p. 2) should be placed in a vacuum with sulphuric acid, care being taken in exhausting the air that the urine does not boil and is not allowed to bubble; from ten to fifteen grammes may in this manner be very readily evaporated in a shallow basin. The application of heat, as, for instance, of the air-bath, is, however, even more objectionable for *drying* the residue than for evaporating the urine; the urinary residue commonly forms a tough, extract-like, and very hygroscopic mass, and hence several precautions are here required, besides those which were noticed in vol. i., p. 340, for drying animal substances. In the first place, the urinary residue ought only to be dried in a vacuum at a mean temperature, because it invariably becomes decomposed on the application of heat, although in some cases more than others. When the urine is heated on an air-bath, as, for instance, at about 90 or 100° C., it always becomes enveloped in an atmosphere which contains ammonia, but which regains its ordinary condition when the air has been frequently changed, and a corresponding loss of weight may be observed on each repeated weighing. The process of weighing is here attended with the greatest difficulties, since the urinary residue is almost more hygroscopical than that of the bile; and on this account the precautions there indicated, or some other means, must be employed to hinder the increase of weight which may be induced by the attraction of water during weighing. It is of little use to place sulphuric acid or chloride of calcium within the case of the balance; but, instead of the shallow evaporating basin, a wide vessel may be employed, having a ground-glass stopper or glass plate, which, immediately after the drying and before the weighing, should be attached to the evaporating vessel. We certainly cannot hope to effect a perfect drying of the urinary residue without the application of artificial heat; but we may, at all events, obtain results by this method which admit of being compared with one another, and which would be unattainable if we employed heat.

Alkaline urine—that is to say, urine containing carbonate of ammonia—is very ill adapted for quantitative analysis. If, therefore, it is deemed necessary to analyse it, it must be neutralised before it is evaporated, or, what is still better, acidified, by means of a definite quantity of dilute sulphuric acid, which must subsequently be accounted for in the analysis.

We have already spoken, in the first volume, under their respective heads, of the various methods adapted for the quantitative determination of *urea, uric acid, hippuric acid, sugar, albumen, oxalate of lime*, &c. Nor have we much to add in reference to the quantitative determination of the *mineral constituents* of the urine beyond what we have already stated of analyses of the ash in vol. i., pp. 405–412. In case we do not wish to adopt Rose's method of determining the ash, the process of carbonizing and incinerating the residue of the urine may be considerably facilitated by adding to the urine, before its evaporation, a quantity of nitric acid nearly equivalent to its urea; by this means nitrate of urea is formed, which becomes decomposed on evaporation into carbonic acid and nitrate of ammonia, and escapes, during further concentration, in the form of water and nitrous oxide. Much time is gained by this method, for the substance which constitutes the larger portion of the urinary residue, and which yields a very large quantity of carbon on exposure to a red heat, is in this manner almost entirely eliminated. It might be feared that a portion of the alkaline chlorides would thus be decomposed either by the nitric acid or the nitrous oxide; but from the direct experiments which I have made with this and with the ordinary method, I find that there is no loss of chlorine unless we add so much nitric acid that slight explosions occur on exposing the solid residue to a red heat. But it is not possible, even by this method, to consume the urinary residue so entirely as only to leave a white ash, if we keep in view that we are attempting a quantitative analysis, and have regard to the vapours of phosphorus and chlorine which escape on intense heating. On account of the presence of soluble and fusible salts, the carbonaceous residue of the urine can scarcely ever be perfectly incinerated, for the particles of carbon become invested by means of the fusible salt with a crust, which protects them from the action of oxygen. As this is the case even with very small quantities of the urinary residue, I regard the following method as the best adapted for quantitatively determining the mineral constituents of the urine: the carbonaceous ash must be weighed with the caution necessary in the case of hygroscopical bodies, and after being washed with water, must be filtered; and the residue on the filter, whose weight in the dry state has been previously ascertained, must be again weighed. The difference of weights gives the amount of the mineral substances dissolved by the water; the insoluble parts may now be easily incinerated, and their quantity thus determined. The further analysis must then be completed by the ordinary methods.

The combustion of the carbon by oxygen in a platinum capsule seems to me, at all events in the case of the urine, to be altogether unsuitable, on account of the volatilization of the chlorine, and even of sulphuric and phosphoric acids.

Chambert's* method is the best adapted for a continuous series of determinations of the mineral substances of the urine. The evaporation of the urine must be effected in the following manner: a tube two centimetres in width is provided, at its lower extremity, with a glass tube, twice bent at right angles, and terminating in a sphere; this sphere again opens into a minute drawn-out glass tube, whilst the upper part of the wide tube passes into a small glass tube into which a cock is inserted. This apparatus is filled with urine, and so secured to the stage of a Berzelius's spirit lamp that the opening of the glass sphere is brought immediately over a heated platinum crucible. By means of the cock we may regulate the access of the air, and the corresponding dripping of the urine into the crucible. Chambert allows the urine to escape so slowly, that one drop is suffered to evaporate before another succeeds it. In this manner 100 or 110 grammes of urine may be evaporated in the course of an hour and a half. Loss by spirting may be tolerably well prevented by carefully and uniformly regulating the escape of the fluid. The layer of carbon which speedily invests the crucible does not amount to the twentieth part of that obtained by the ordinary method.

In order to effect the combustion of the residuary carbon, distilled water should be suffered to drop on the glowing carbon from the same reservoir in which the urine was previously contained; the combustion of the carbon will go on with tolerable rapidity at those points with which the water comes in contact, owing to the well-known decomposition of this fluid at a red heat; but as some carbon will always adhere to the walls, it must repeatedly be removed, and more water allowed to drop upon it. The experiment does not gain in accuracy by this method, but the combustion is effected with greater rapidity. Hence we may perceive that, although this analysis is very applicable in certain cases, it cannot, for many reasons, lay claim to any great degree of exactness.

It is obvious from the above remarks, that the composition of

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* Recueil des Mémoires de méd. et de pharm. militaire. T. 58, p. 328.

the urine in certain physiological and pathological conditions can only be correctly determined when the quantities of the urinary constituents daily secreted by the kidneys can be compared together. We will, therefore, in the first place give the *quantitative relations* which occur under different conditions in the collective urine which has been secreted within definite periods of time.

Lecanu* found that sixteen persons of different ages and sexes, but who all received a due supply of mixed food, passed in twenty-four hours from 525 to 2271 grammes of urine; while Becquerel found that the mean daily quantity passed by four men was 1267·3 grammes, whilst that by four women was 1371·7 grammes. Chambert, who made twenty-four observations on men between the ages of twenty and twenty-five years, found that the daily quantity of urine varied from 685 to 1590 grammes. In experiments which were, for the most part, made in the summer, I discharged, during a fortnight's strictly regulated diet, from 898 to 1448 grammes of urine daily; during twelve days, on which I lived exclusively on animal food, from 979 to 1384 grammes; and during a twelve days' course of vegetable diet, from 720 to 1212 grammes.

We have already spoken of the dependence of the *quantity of water* which is separated by the kidneys, on the amount of drink that has been taken, and on the degree of transpiration. Unfortunately, we have as yet no accurate experiments to demonstrate the influence which each of these physiological causes exerts on the amount of water that is separated by the kidneys. The facts communicated by Julius Vogel,† who, for 189 days, weighed all the food and drink that were taken by a person on whom he was experimenting, show how much other influences, besides the fluids that have been taken, modify the quantity of water in the urine. Whilst on some days scarcely the third part of the fluids that had been taken were carried off by the urine, on other days the quantity of the urine equalled that of the drink, or even exceeded it by one-twentieth, or even one-tenth. The largest quantity of water was unquestionably discharged by the kidneys after the use of a cold bath; here there was not only suppressed transpiration, but water was absorbed from without.

It appears, from the observations of Chambert, that shortly after a meal, less water, both absolutely, and relatively to the solid constituents, is separated with the urine. Closely allied to this

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* Journ. de Pharm. T. 25, p. 681 et 746.

† Wagner's Physiol., S. 264 [or English Translation, p. 421].

point is the first of the questions propounded by Lecanu, whether, when the kidneys are secreting an excess of water after copious drinking, they, at the same time, separate an excess of solid constituents; Lecanu answers this question in the negative, although my own experiments lead to an opposite conclusion, as do also those of Chossat* and Becquerel.

This is obviously a question to be settled by bedside experience; we can hardly, however, agree with Becquerel in believing that it will explain the mode of action of many diuretics.

Before proceeding to enumerate the quantities of the solid constituents of the urine which are daily secreted, I must not omit to mention the very great differences between the statements of those who have investigated this subject. This difference depends only in a very slight degree on the different methods of chemical investigation and calculation; it is mainly due to the individuality of the different persons, we might almost say of the different nations, on whom the experiments had been instituted. On comparing the urinary analyses that have been made by experimentalists in the three great nations, we perceive that, generally speaking, far the least solid constituents are found in the urine of the French, and that they are especially deficient in urea and uric acid, that the Germans very far exceed the French in these respects, while again the English pass even larger quantities than the Germans. One of the principal grounds of this difference is, no doubt, to be sought in the difference of diet, and in the varied modes of life of the three nations. It is well known that the French take very little animal food, and live generally with great moderation, while the English use highly seasoned animal food so abundantly that Prout† not unfrequently met with specimens of urine from which nitrate of urea at once crystallized on the addition of nitric acid,—a circumstance that would hardly occur to a genuine German urine, to say nothing of French specimens. From statistical data it appears that any given number of Londoners eat six times as much animal food as an equal number of Parisians. Besides the nature of the food, there are doubtless other, although probably less influential causes for such differences, as, for instance, the general mode of life in other respects, the climate, &c.

With regard to the *solid constituents* which are daily separated

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* Journ. de Physiol. T. 5, p. 65.

† [We are not aware that Prout has described any cases in which he has seen *healthy* urine undergo this change.—G. E. D.

with the urine, the following are the final results obtained from several series of experiments: Becquerel found (from experiments on four men and four women) that 39·52 grammes of solid matter are, on an average, secreted daily by the kidneys of men, and 34·31 grammes by those of women. While living on a mixed diet, I discharged, on an average, 67·82 grammes in twenty-four hours; on an exclusively animal diet, 87·44 grammes; on a vegetable diet, 59·235 grammes; and on non-nitrogenous food, 41·68 grammes. Lecanu found that men secreted far more solid matters by the kidneys than women, old men far less than women, children eight years old more than old men but less than women, and lastly, children four years old even less than old men.

We have already spoken, in the first volume, of the proportions in which the most important of the solid constituents of the urine stand to one another, as well as of the quantities which are daily secreted. (See vol. i., p. 162, for urea; p. 211, for uric acid; and p. 195, for hippuric acid.

According to Becquerel, the daily amount of *extractive matters* (that is to say, of the organic matters exclusively of the urea and uric acid) averages 11·738 grammes in men, and 9·655 grammes in women; while living on a mixed diet, the quantity of these matters which I daily secreted, amounted to about 13 grammes.

The quantity of the *fixed salts* varies extraordinarily in different persons, living different modes of life. The following are the daily quantities of fixed salts which were discharged in the specimens of urine analysed by Lecanu:—

	The average.	Fluctuations between
In men	16·88 grammes.	9·96 and 24·50 grammes.
In women	14·38 ,,	10·28 ,, 19·63 ,,
In children	10·05 ,,	9·91 ,, 10·92 ,,
In aged persons	8·05 ,,	4·84 ,, 9·78 ,,

According to Becquerel, the mean quantity of fixed salts daily secreted by the kidneys in men is 9·751 grammes, and in women 8·426 grammes; while Chambert, from analyses of the urine of twenty-four young men, fixed it at 14·854 grammes, its limits being 23·636 and 6·993 grammes. In my own urine, I found that while living on a mixed diet, the average quantity was 15·245 grammes, the extremes being 17·284 and 9·652 grammes.

Lecanu found that the quantities of phosphate of lime which are daily given off by the kidneys varied between 0·029 of a gramme and 1·960 grammes. I have never observed such great fluctuations either in my own urine, or in that of other healthy persons, during an ordinary or even an exclusively animal or vegetable diet. The influence of the food upon the quantity of earthy phosphates in the urine is, however, undeniable; while, living on a purely animal diet, I found that my urine contained nearly three times as much earthy phosphates as when living on a mixed diet. The urine of young children, like the allantoic fluid of calves, contains only very small quantities of phosphates, but a comparatively large amount of sulphates. It is probably for some similar physiological reason that pregnant women secrete far less phosphate of lime with the urine than non-pregnant ones,—a fact that has been previously mentioned.

These few illustrations are sufficient to indicate the numerous conditions on which the quantities of the urinary constituents and their various proportions to one another are dependent, and to show the caution we should exercise in forming an opinion on the nature of a specimen of urine, or in drawing any conclusions on the point, unless we have numerous analyses of different urines collected under similar conditions.

The next point which it is necessary for us to notice, is the difference in the urine *in the two sexes.* From the experiments of Lecanu and Becquerel, to which we have already alluded, it appears that the chief difference is, that the urine of women contains more water and less urea and salts, even in relation to the other solid constituents; that is to say, women discharge absolutely more water and far less urea and salts than men, while the quantity of uric acid appears to be about the same in both sexes.

The urine of women in a state of *pregnancy* presents certain marked peculiarities, of which the most distinguishing, namely, the formation of the substance called kyestein, has been already noticed in p. 426. Becquerel found that the specific gravity during pregnancy never exceeded 1·011. According to Lubanski,* such urine contains less than the ordinary quantity of free acid, and is frequently neutral or even alkaline; as far as my own experience goes, it is, however, always acid when freshly passed, if the women are in good health, but during the latter months of pregnancy it very readily becomes alkaline, since it then generally becomes more aqueous. We have already alluded to the relative and absolute diminution of the phosphate of lime in the urine of pregnant women.

We are indebted to Lecanu for most of our knowledge regarding

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* Ann. d'Obstetr. &c. 1842, p. 235.

the influence which the different *periods of life* exert on the constitution and the quantitative relations of the urine. It appears generally from his observations, that men in the vigour of early adult life, when the metamorphosis of tissue is proceeding most actively, secrete the largest quantity of solid constituents with the urine; that women secrete somewhat less, and children and aged persons still smaller quantities. The period of life appears to exert no influence on the quantities of the uric acid and of the salts. From certain experiments, it would appear that the urine of very young children contains relatively more hippuric acid and far less phosphate of lime than the urine in more advanced life.

Of all the physiological conditions, the food is unquestionably that which exerts the most marked influence on the constitution of the urine. We have already spoken, in various parts of this work, of the influence which special substances contained in the food exert on the acid or alkaline reaction of the urine, and on some of its constituents. In the prolonged series of experiments, to which I have often alluded, I have attempted to ascertain the influence which varieties of diet (animal, vegetable, and non-nitrogenous) exert on the character of the urine generally, and on its special quantitative relations. The most essential results may be seen at a glance in the following tabular arrangement. While living on a mixed diet and adhering as closely as possible to the same dietetic conditions, I made the analysis of the collected urine; while living on a purely animal diet (almost exclusively on eggs), I made twelve observations, and a similar number while living on a purely vegetable diet; and while living on perfectly non-nitrogenous food (fat, milk-sugar, and starch) I made two analyses; and, independently of the variable quantities of water, the following were the mean quantities (in grammes) of the other substances which were discharged in the twenty-four hours' urine:—

	Solid constituents.	Urea.	Uric acid.	Extractive matters and salts.
On a mixed diet	67·82	32·498	1·183	12·746
On an animal diet	87·44	53·198	1·478	7·312
On a vegetable diet	59·24	22·481	1·021	19·168
On a non-nitrogenous diet....	41·68	15·408	0·735	17·130

From these researches we may draw the following general conclusions:—

(1.) The solid constituents of the urine are very much increased by animal food, while they are considerably diminished by a vegetable diet, and still more so by a non-nitrogenous one.

(2.) Although the urea is a product of the effete and decomposed tissues of the animal organism, the quantity in which it occurs in the urine depends in part upon the nature of the food that has been taken; during a highly nitrogenous animal diet, the quantity of urea is absolutely increased, while, on a vegetable as well as on a positively non-nitrogenous diet, it is absolutely diminished. Moreover, the relative quantity of urea, as compared with the other solid constituents of the urine, increases, or diminishes, with the nature of the food. During a mixed diet, I found that in my own urine the ratio of the urea to the other solid constituents was as 100 : 116; during an animal diet, as 100 : 63; during a vegetable diet, as 100 : 156; and during a non-nitrogenous diet, as 100 : 170.

(3.) The quantity of uric acid in the urine depends much more on other conditions, and possibly on other substances introduced into the organism, than on any peculiarity of diet. The differences observed during these observations were too small to allow of our concluding that the nature of the food exerted any essential influence on the formation of uric acid.

(4.) When the protein-compounds, and, consequently, the nitrogen of the animal food, are absorbed in excess in the intestinal canal, that portion of them which is not applied to the reproduction of the consumed tissues, undergoes metamorphosis, and, at last, is again rapidly separated by the kidneys in the form of urea and uric acid. It is only through the kidneys that the animal organism gets rid of any excess of nitrogen which may be absorbed.

(5.) The sulphates and phosphates which are discharged correspond very nearly in quantity with the nitrogenous matter that has been taken, that is to say, with the protein-compounds, which contain sulphur and phosphorus; after the almost exclusive use of protein-compounds, the quantity of these salts in the urine is considerably increased.

(6.) It follows from these propositions, that the other organic constituents of the urine, that is to say, the extractive matters, must be very much diminished during an animal diet; we find, from our investigations, that after the use of vegetable food, there is an absolute (not a mere relative) augmentation of such substances—a proof that vegetable food contributes largely to the formation of the extractive matters of the urine. Further, after the use of animal food, the physical properties of the urine precisely resemble those of this secretion in the carnivora; that is to say, the secretion is of a very light amber-yellow tint or almost straw-coloured, has a strong acid reaction, and appears either to contain no lactic acid, or only a very small quantity, while, according to Liebig's experiments, it also appears to be perfectly devoid of hippuric acid. On the other hand, after a course of vegetable diet, a very great portion of the free acid is lost, and during a non-nitrogenous diet it altogether disappears: it contains a large amount of dark-coloured extractive matter, and hence is of a brownish red tint; it is also somewhat turbid, from the separation of earthy phosphates, or at all events, readily becomes so on boiling; it almost always contains alkaline lactates, with oxalate of lime; according to Liebig, it is tolerably rich in benzoic acid; as is obvious, from the preceding table, I have never found the uric acid completely absent.

The influence of *indigestible or highly seasoned food, of alcoholic drinks, &c.*, on the augmentation of the uric acid in the urine, has been already noticed in vol. i., p. 213.

The fact that, after prolonged fasting, the urine becomes strongly acid, and poor in solid constituents, but that it always contains some urea, has been already mentioned, and is in part numerically demonstrated in vol. i., p. 163.

It follows, from my own and Simon's experiments,* that after *violent bodily exercise* far less water is separated by the kidneys, but that the quantities of free acid, of urea, of phosphates, and of sulphates, in the twenty-four hours' urine, are increased, while those of the uric acid and of the extractive matters are diminished.

It is scarcely necessary to mention that the quantity of water separated by the kidneys must be influenced by *the season of the year, the climate,* and *the atmospheric temperature;* for the most superficial observer can notice this in his own person. Julius Vogel has, however, definitely proved it, by weighing daily for six months the urine that was discharged by the same individual. I believe that my experiments (noticed in vol. i., p. 213) completely overthrow the opinion maintained by Fourcroy, Marcet, and Schultens, that prolonged *sweating* increases the quantity of uric acid in the urine.

The urine first passed after the night's rest, the *urina sanguinis,* is, as is well known, of greater density, a darker colour, and a

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* [We may also refer the reader to Percy's experiments on this point, recorded in p. 169 of the second volume of the translation of Simon's Animal Chemistry. G. E. D.]

somewhat stronger acid reaction, than that which is passed during the day. The quantities of this *morning urine* vary with the amount of drink that has been taken before retiring to rest. Independently of the smaller quantity of water which it contains, I can detect no difference in the ratio of its constituents to one another. The nature of the food exerts a certain amount of influence on the morning urine; at all events, while living on animal food, I found it comparatively even more concentrated than the urine passed during the day; even after living for only a single day on purely animal food, I found that on the addition of nitric acid to the urine passed on the following morning, nitrate of urea was at once separated.

Another kind of urine, that, namely, of *digestion,* or the *urina chyli,* was formerly regarded as a distinct variety, to which much weight was attached; in those who do not drink much at, or after, their meals, it is somewhat denser and more coloured than that which is passed at other periods of the day; it is, however, not so coloured or so dense as the morning urine.

Chambert's experiments, which appear to have been very carefully conducted, do not altogether coincide with my own: the differences are, however, such as may be readily explained by surrounding circumstances. Chambert invariably found the urine of digestion denser and richer in salts than the morning urine; the greater or lesser transpiration during sleep, and the varying amount of drink taken at meal-time, afford the simplest clue to these differences. Moreover, Chambert found that the inorganic constituents of the urine stand in a direct proportion to the quantity of the salts taken in the food.

In the twenty-four hours' urine Chambert found on an average 1·3024% of salts, in the urine of digestion 1·6394%, and in the urine discharged between waking and breakfast 0·9332%, while in the urine soon after drink had been taken, the maximum was only 0·2113%.

In animals, at all events, in the *mammalia,* the influence of the food is reflected in the constitution of the urine. We will now proceed to notice the urine of animals, classifying them according to the nature of their food.

Unfortunately, our knowledge of the urine of the *omnivora* is confined to that of the man and the *pig.* The urine of the latter animal has been examined by Boussingault* and von Bibra†; it is perfectly clear, almost devoid of odour, distinctly alkaline,

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* Ann. de Chim. et de Phys. 3 Sér., T. 15, p. 97—104

† Ann. d. Ch. u. Pharm. Bd. 53, S. 98—112.

effervesces with acids, and becomes turbid on boiling, which converts the earthy bicarbonates into simple carbonates, which, consequently, become precipitated; it does not contain ammonia; neither Boussingault nor von Bibra could discover either uric, or hippuric, acid in it; but Boussingault has shown that in all probability it contains alkaline lactates. Phosphates occur only in very small quantity in it, but sulphates and chlorides are tolerably abundant. The specimens of pigs' urine examined by these chemists contained from 1·804 to 2·086% of solid constituents, in which from 0·29 to 0·49 were urea.

The urine of *carnivorous animals* differs only slightly from that of man; when freshly passed, it is of a light yellow colour, of a disagreeable odour, a nauseous bitter taste, and an acid reaction; it very soon, however, becomes alkaline. Vauquelin,* Gmelin, Hünefeld, and especially Hieronymi,† have examined the urine of lions, tigers, leopards, panthers, hyænas, dogs, wolves, and bears. Urea is present in the urine of these animals in large quantities, and may be separated in a state of great purity, since only little pigment is present: uric acid is only present in it in very small quantity; Landerer,‡ however, found 1% of uric acid in the urine of the hedgehog (Erinaceus europæus).

The urine of the *herbivora* is very different from that of the carnivorous animals and of man. This secretion has been examined in the case of elephants, rhinoceroses, camels, horses, oxen, goats, beavers, rabbits, hares, and guinea-pigs; it is generally of a yellowish colour, very turbid, of an offensive odour, and is always alkaline; it certainly resembles the urine of the carnivora in often containing much urea, but it differs from the latter in containing a considerable amount of alkaline and earthy carbonates, and of a fatty and odorous matter, in the perfect absence of uric acid, and in its extremely small quantity of earthy phosphates. According to Boussingault, lactates are always present.

The *urine of the horse* has been more carefully studied (by several chemists) than that of any other animal of this class; like that of man, it varies with the nature of the food; when freshly passed, it is usually turbid and of a pale yellow colour, but on exposure to the air it very soon assumes a dark brown tint; in the course of my experiments I have sometimes found it tolerably clear, and it then had a strong alkaline reaction; besides alkaline bicarbonates, it contains in solution a very little of the bicarbonates of lime

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* Ann. de Chim. T. 82, p. 174.

† Jahrb. d. Ch. u. Phys. Bd. 3, S. 322.

‡ Arch. f. Ch. u. Mikros. Bd. 3, S. 296.

and magnesia, which separate from the fluid on boiling; it often, however, has a faintly acid reaction, and then we have true *urina jumentosa,* from the deposition of earthy carbonates. Bibra often found great and altogether unaccountable differences in the urine of horses fed in precisely the same manner. The potash in this urine naturally preponderates considerably over the soda. In the sediment of horses' urine I have always found the most beautiful crystals of oxalate of lime in very considerable quantities. Bibra, however, in examining the sediment of a horse's urine, found also a special organic substance, which he could not accurately examine, in addition to the carbonates of lime and magnesia. Attempts have been made to explain the occasional presence of benzoic acid, which is assumed sometimes to take the place of hippuric acid in horses' urine under certain physiological, or pathological, conditions; it is, however, I believe, now established beyond all doubt that the view originally supported by Liebig, regarding the frequent occurrence of benzoic acid in the urine of horses, is correct (see vol. i., p. 83). In the urine of diseased horses I have likewise always found hippuric acid, if it was examined while still fresh. No traces of the salts of ammonia can be detected in horses' urine. Sometimes in examining horses' urine we find that in place of hippuric acid there is a nitrogenous, uncrystallizable, resinous matter which has not yet been accurately examined. (C. Schmidt.)

In the urine of a diseased horse I found so large a quantity of lactate of potash, that the lactic acid could be combined with lime, magnesia, and oxide of zinc, and could be recognised with certainty by its salts.

It stands to reason that the characters of the urine must vary extremely during the diseases of animals. I extract, by way of illustration, the following examples from my note-books. A very lean, badly conditioned Wallachian horse, fourteen years old, had suffered for a week from pneumonia of the right side; the urine was of a very pale yellow colour and scarcely at all turbid; it was viscid and somewhat ropy, was strongly alkaline, but did not effervesce on the addition of acids it remained yellow on evaporation, contained only very little hippuric acid, &c. Another Wallachian horse, thirteen years old, was suffering from acute glanders; it was fed, as was the horse in the previous case, upon bran, hay, and straw; the urine was of a well-marked reddish brown colour, was faintly alkaline, and contained a very considerable sediment of the carbonates of lime and magnesia; the fluid, after the removal of the sediment by filtration effervesced strongly with acids, became of a reddish brown and almost of a black colour on evaporation, contained a large quantity of hippuric acid, &c. A very powerful cavalry horse, seven years old, and fed upon hay, oats, and straw, passed a brownish yellow, very alkaline urine, which contained only a small amount of earthy carbonates; the same horse, when fed upon oats and straw, without hay, discharged urine which was very turbid from the presence of earthy carbonates, whose reaction was scarcely alkaline, and which, when filtered, did not effervesce with acids.

The *urine of cattle* has been frequently analysed by Boussingault and v. Bibra. On examining it shortly after its discharge, I have always found it clear, of a bitter taste, a pale yellow colour, and with a strong alkaline reaction: it contains much sulphate and bicarbonate of potash and magnesia, but very little lime; according to Boussingault, it contains no phosphates, very little chloride of sodium, but on the other hand, a large amount of lactate of potash; according to v. Bibra, the quantities of urea and hippurate of potash are liable to great variations, even when the feeding and external conditions remain unchanged. I have always found oxalate of lime in the sediment, but, like Boussingault, I have never been able to detect ammoniacal salts in the fresh urine of oxen. This urine generally contains from 8 to 9% of solid constituents, of which from 1·8 to 1·9% are urea. The hippuric acid varied, according to v. Bibra, from 0·55 to 1·20%. Boussingault found free carbonic acid gas in it, in addition to alkaline bicarbonates.

The *urine of calves* differs very much from that of cattle, and approximates more in its composition to the allantoic fluid of the fœtus. It appears from the investigations of Braconnot and Wöhler,[†] that the urine of calves, as long as they are sucking or are fed on milk, is almost colourless, clear, devoid of odour, of very little taste, and with a strong acid reaction, which it does not lose even on evaporation. Wöhler's discovery, that allantoine is the principal organic constituent of this urine, has been already noticed in p. 175 of the first volume. According to Wöhler, it appears, further, to contain urea and likewise *uric acid*, in the same proportions as they occur in normal human urine; hippuric acid, on the other hand, cannot be discovered in it. It contains a very considerable amount of phosphate of magnesia and of the potash salts, but only very small quantities of the phosphates, sulphates,

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[*] Ann. de Chim. et de Phys. 3 Sér. T. 20, p. 238—247.

[†] Nachr. d. k. Gesellsch. d. Wiss. zu Göttingen. 1849. No. 5, S. 61—64.

and soda salts. Braconnot also found in calves' urine an organic matter which was soluble in alcohol, precipitable by tannic acid, dissolved on boiling, but again separated on cooling. Lastly, this secretion does not contain even 1% of solid constituents; according to Braconnot, they amount to 0·62%.

The *allantoic fluid* of the fœtal calf has, as yet, only been carefully analysed by Lassaigne;[*] from his observations, it seems to possess precisely the same properties and the same composition as the urine of the calf, while still living on milk.

We have already mentioned that the urine of *rabbits,* as w el probably, as that of other herbivorous animals, becomes acid, and assumes almost all the properties of the urine of the carnivora, when these creatures have been kept fasting for a long time, or have been compelled to digest animal food.

Hyraceum appears, from Reichel's analysis, to be at all events very much mixed with the urine of the animal (Hyrax capensis): but from a microscopical and chemical examination, to which I exposed a specimen of this substance, whose therapeutic value was to be tested, I convinced myself that it consists solely of the solid excrement of this creature; I found in it the remains of plants and vegetable fibres, together with isolated prosenchyma cells and spiral vessels, which rendered it more than probable that the vegetable matters had passed through the intestine, and were not either accidentally or intentionally superadded after its discharge; it was only on the outer surface that fragments of the skeletons of insects could be detected, stamped, as it were, upon it: in addition to a very large amount of resinous matters and carbolic acid, this mass undoubtedly contained biliary matters; but no urea, or uric, or hippuric acid could be discovered.

The urine of *birds,* which for the most part forms a whitish investment to the solid excrements of these animals, consists essentially of urates, and especially of the bi-urates of ammonia and lime; Coindet maintains that he has found urea in birds' urine.

The urine of *serpents,* which is often discharged independently of the solid excrement, is at first pulpy, but soon becomes solid and dry; it consists for the most part of alkaline bi-urates, a little urea, and earthy phosphates.

The urine of *frogs* is fluid; it contains urea, chloride of sodium, and a little phosphate of lime.

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[*] Ann. de Chim. et de Phys. 1 Sér. T. 17, p. 301.

The urine of *tortoises* has been examined by Magnus, Marchand, and myself. (See vol. i., pp. 196 and 212.) I found the urine of Testudo græca to possess the following properties and composition: when the animals had taken no food for a long period, they discharged (when lying on their backs) a very pale yellowish green clear urine, with a distinctly acid reaction; on cooling, it deposited a white sediment, which redissolved on the application of heat; when they had not fasted for a long time previously, they discharged a neutral or faintly alkaline, tolerably clear urine, which exhibited no turbidity on cooling. The spontaneous sediment dissolved only partly in boiling water, the bi-urates of ammonia and lime remaining undissolved, while the bi-urate of soda dissolved. The presence of hippuric acid could always be detected with great facility in the urine of these animals by either of the methods described in vol. i., p. 194.

Besides urea and the above named substances, I also found a crystallizable organic matter, that was insoluble in absolute alcohol, but dissolved in alcohol of 82%; but in consequence of the small quantity in which it occurred, I could not minutely investigate it. Fat was always present in appreciable quantity. The acid sedimentary urine contained from 3·014 to 3·584% of solid constituents; the average amount of the ash of the solid residue was 52·5%; when burnt white, it contained no carbonates, but only phosphates and sulphates with chlorides; it further contained more potash than soda compounds.

The excrements of *insects* consist, for the most part, of the remains of the tissues which have served them for food, but they also contain materials which are nowhere else found than in true urine, even when no definite organ for the elaboration of this secretion can be detected in them.

It has long been known that the red *excrements of butterflies* contain a very large amount of alkaline urates, and the fact has been recently confirmed by Heller. I have found that the intestinal contents of butterflies that have been sucking honey often contain free uric acid in very beautiful crystals. The red pigment of the excrement is an oily body, which, when placed in water, separates in minute drops; in addition to these substances, a little phosphate and oxalate of lime are also present in these excrements.

In the *excrements of caterpillars*, vegetable fibre is naturally the preponderating constituent, but they also contain large quantities of chlorophylle and starch; the latter is found not only in the globular form, but also in the peculiar baton-like shape in which it occurs in the Euphorbiaceæ. These excrements are especially rich in oxalate of lime, which is not produced directly from the ingesta; for I have found them in the biliary tubes of caterpillars. Although the intestinal juices and the contents of the stomach of caterpillars have always a very strong alkaline reaction, the excrements are for the most part neutral, and indeed sometimes have an acid reaction. In the latter case, we often find that they contain very beautiful crystals of uric acid; the uric acid, however, generally only appears in very small quantity in the excrements of caterpillars. Different parts of plants, as, for instance, the spiral vessels, may be very distinctly observed in these excrements, which are so poor in nitrogen that, as an average of three analyses, I found only 0·362$\frac{0}{0}$ of this element in the matters discharged by the silkworm, while the leaves of Morus nigra contained 4·560$\frac{0}{0}$.

We have already spoken, in vol. i., p. 173, of the occurrence of guanine in the excrements of spiders. Seeing that this substance is present here as well as in guano, it is not improbable that guanine may also occur in the excrements of birds and in those of most insects, especially since the researches of Will and Gorup-Besanez* have rendered it probable that this substance is also present in the green organ of the craw-fish.

Guano, that much-prized article of commerce, which is the product of the slow decomposition of the excrements of certain sea-fowl, has been very frequently analysed, and has been found to be very variously composed according to the place from whence it was obtained; its principal constituents are guanine, urate of ammonia, oxalate of ammonia, phosphate of lime, phosphate of magnesia and ammonia, and oxalate of lime; we likewise find the remains of vegetable substances; and there is one variety which contains the most beautiful siliceous shields of infusoria pertaining to the Bacillariæ.

We now proceed to the changes which the urine undergoes in disease; and we will first notice the characters which are impressed upon this secretion in *fever*, that is to say, in that group of symptoms which accompany almost all acute diseases. Febrile urine is generally more deeply coloured than usual (being of a red or reddish tint), has a stronger odour, a higher specific gravity, and a more decided acid reaction. As long as the fever continues, less than the normal quantity of urine is generally secreted by the

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* Gel. Anzeigen d. k. bair. Ak. d. Wiss. 1848. S. 825—828.

kidneys, and the urine appears concentrated, because the diminution of the water of febrile urine is relatively more considerable that the diminution of the solid constituents.

The constant characters of such urine are the relative and absolute diminution of the inorganic salts, and the obvious augmentation of the uric acid or urates. The diminution of the salts was always observed by Becquerel and Simon; it was the latter chemist who first discovered that the loss principally fell on the the chloride of sodium. Even when febrile urine does not deposit the ordinary sediment of urate of soda, it is always absolutely and relatively richer in uric acid than other urine. The urea is generally somewhat diminished, as Becquerel first demonstrated; Simon holding the opposite view. The extractive matters are usually somewhat increased. Lactic acid may very often be detected with chemical certainty in urine of this nature.

In contrast to febrile urine, Becquerel has distinguished an *anæmic* urine. Such urine, which depends upon a deficiency of blood, and occurs in various forms of debility, contains far less urea and uric acid than normal urine: the diminution of the salts, as compared with the quantity usually secreted, is inconsiderable; the salts are consequently increased in relation to the organic matters; moreover, the extractive matters only differ slightly from the physiological average. This variety of urine is especially observed after repeated venesections, and in chlorosis.

If we endeavour to name and distinguish the constitution of the urine in individual diseases, in accordance with the present condition of pathology, and to collect and arrange the results of the numerous investigations which have been made on this subject during the last twenty years, we are led to the unexpected and discouraging conclusion, that all our knowledge regarding it is alike incomplete and obscure. The innumerable analyses of morbid urine have induced many physicians to believe that the study of the character of the urine in diseases was the most complete section of pathological chemistry,—an error which has been promulgated, whether consciously or unconsciously, even by chemists. Where are we to seek the reason of a fact at once so mortifying and discouraging to the pathological chemist? In reply, it may be answered, that there are several grounds on which we might explain the want of success which has so frequently attended the most earnest endeavours of numerous able inquirers. It has already been frequently noticed, both here and elsewhere, that the methods employed in these investigations were not of such a nature as to justify the establishment of those conclusions and general propositions which were deduced from the results of the analysis; in the methodological introduction to the first volume, we drew attention to the errors, and the different causes which have given rise to these false deductions. A truly scientific examination of the urine is, however, associated with numerous obstacles and difficulties, and failure may thus frequently attend our efforts, even when all the methods have been employed which present themselves for the prosecution of such an important investigation. The object of such inquiries is obviously that of ascertaining the general properties of the urine and its especial composition in any one definite form of disease; for the urine, even in health, and still more in disease, is of so variable a nature, that in many cases it is impossible to determine whether the alterations noticed in its condition actually arise from a morbid process, or only from incidental influences. If we carefully observe the changes which often occur in the urine in the course of the same day, not merely in typhus or any abnormally developed acute exanthema, but also in inflammations which are running their ordinary course, we shall clearly see that the urine is regulated much more closely in accordance with the transient condition of the organism, external influences, and simultaneously manifested groups of symptoms, than by the nature of the morbid process. Thus the albumen in the urine in Bright's disease is considerably diminished, and may even almost disappear, if the chronic form of this disease is associated with an affection giving rise to inflammatory fever. The urine which is so characteristic of this form of disease, loses almost all its distinctive properties, and assumes, both in a qualitative and quantitative point of view, the character of inflammatory febrile urine. It appears to us, therefore, to be more rational to limit our examination of the composition of the urine to certain morbid conditions and individual groups of symptoms, and to compare together the various analytical results thus obtained, instead of attempting to extend similar observations to different forms of disease. This method of proceeding is exemplified in the numerous analyses of the urine conducted with such extraordinary perseverance by Becquerel; for the results of these admirable observations prove less that certain groups of diseases are associated with definite alterations in the proportions of the solid constituents, than that most diseases are attended by very considerable fluctuations in the composition of the urine, depending more upon incidental individual phenomena than upon any special morbid process.

Although the blood may not unfrequently undergo more marked changes from secondary causes than from any essential, morbid process, it retains a stronger impression of these modifications than the urine. This difference may probably depend upon the blood preserving the capacity, even in a morbid condition, of throwing off effete matters, if not by the kidneys, by some other medium, whilst the urine retains everything that may have been incidentally generated in the blood and conveyed to the kidneys.

But although these and many other relations may have opposed the efforts of inquirers to discover any constantly recurring properties and admixtures of the urine in individual acute diseases, it might have been hoped that more promising results would have rewarded their labours in the case of chronic disorders, where the change of symptoms is not so rapid as in acute forms of disease. But here, too, our expectations are not realised, chiefly because the deviations from the ordinary composition of the urine are in general more inconsiderable in these conditions than the modifications which depend upon purely physiological relations, such as the nature of the food and other dietetic relations generally. In reply to the question, whether we have actually discovered any distinctive characters in the urine of tuberculous, cancerous, or arthritic patients, it must be admitted that although numerous conjectures have been suggested which bear the semblance of affording empirical results, we have acquired no facts based upon scientific and exact observations. Thus, for instance, according to Donné, the urine in tuberculosis exhibits a viscid mass of honey-like consistence after evaporation, when seen under the microscope; but has not a similar appearance been observed in other urine? According to some observers, arthritic urine is characterised by an abundance of uric acid; according to others, by a deficiency, or even an absence, of this constituent. Although this striking discrepancy may be referred to the vagueness of the term Arthritis, and to an error of medical diagnosis, hundreds of instances might be enumerated in which results scarcely less discrepant have been established by one and the same observer.

We have here enumerated substances which only occur abnormally in the urine. Are not these characteristic of individual pathological processes? Albumen, fibrin, oxalate of lime, &c., are not characteristic of specific groups of diseases, but merely of individual processes or groups of symptoms accompanying disease; we have already endeavoured to show the numerous conditions which may influence the transition of albumen into the urine, and that these relations may occur in the most various forms of disease. The once prevalent idea that albuminuria was a specific disease, instead of being only a symptom of different diseases, is not entirely exploded.

But there likewise exist abnormal substances in the urine, which differ so widely from the substances commonly contained in that fluid, or in the animal organism generally—as, for instance, red, green, and blue pigments, cystine and xanthine—that they would appear to indicate the existence of some definite pathological process or some specific form of disease. Such may indeed be the case, but all who have observed the occurrence of these matters must be aware that none of these rarely observed substances have been found to appertain to any special form of disease.

Amidst the confusion which prevailed in pathological chemistry as to the composition of the urine in special diseases, the ingenious idea suggested itself to certain inquirers of inventing entirely new diseases in accordance with the constitution of the urine, and the nature and quantity of the various substances which it contains, instead of determining the composition of the urine with reference to the disease. These diseases were named the uric and oxalic acid diatheses, the urea diathesis, &c. Observers thus fell into the same errors of which the older physicians had been accused; namely, that of classifying diseases in accordance with individual symptoms, instead of grouping them in natural families based upon distinct processes rather than symptoms. As we have already frequently expressed our dissent from the assumption of any such diatheses, it would be superfluous again to revert to the subject. But, in opposition to this, it might be asked, is not diabetes mellitus a diathesis? and is it not generally assumed to be a special disease? According to our view, this phenomenon is only a symptom, standing in a causal connection with a definite series of symptoms, in the same manner as many other symptoms are also associated with their respective phenomena. Thus, if in consequence of any anomaly in the metamorphosis of animal matter, from a mechanical or physiological obstruction, the conversion of the sugar in the blood should be impeded, it will be very rapidly separated by the kidneys, as Bernard, Kersting, and myself have proved by direct experiments; this separation cannot, however, be effected, as we have already seen in experiments on animals, without the abstraction of a large quantity of water; the blood becomes poor in water, and hence arise the thirst, the suppressed cutaneous transpiration, and the parchment-like skin of diabetic patients. We almost invariably find, on examining the bodies of patients who have died from diabetes, that certain pathologico-anatomical changes are present; but how widely do these differ in character? As is well known, tubercles are frequently present in the lungs in diabetes, and also, in some cases, affections of the abdominal organs, the spinal cord, &c. Sugar in the urine is therefore as much an incidental, inconstant accompaniment of tuberculosis as albumen in the urine is of dropsy; the former, like the latter, seems always associated with definite conditions, such as we have endeavoured to explain in the case of the albumen present in the urine in dropsy, but which we are unable to explain in the case of the sugar contained in the urine in tuberculosis. Dropsy, however, is as much a mere group of symptoms as tuberculosis; and we must leave it to a future era in medicine to classify diseases in families and species according to definitely expressed chemico- and physico-physiological processes, instead of grouping them according to individual pathologico-anatomical or chemical characteristics.

After our remarks upon the constitution of the urine in the recognised groups of disease, we think it would be superfluous to enter upon the further consideration of the properties and composition of the urine, or the changes which this fluid experiences in every individual disease; for we have already, as far as the present state of science permitted, classified the alterations occurring in the morbid urine, in accordance with chemical modes of arrangement. We must leave this subject for the present, trusting that the attempts which will be made in our third volume to discover the physiological processes in the healthy and diseased animal organism from the positive results of physical and chemical investigations of the animal tissues and juices, may contribute towards the establishment of definite characteristics of the urine as a means of classifying families and groups of diseases.

Owing to the want of systematic investigations of normal and abnormal urine, and the inconsiderable progress made in organico-chemical analyses, a very high value was formerly attached to the analyses of urinary concretions, and of calculi generally. When considered from a scientific and pathological point of view, we are as unable to admit the idea of a Lithiasis as of the above-mentioned diatheses; it lies entirely beyond the scope of our inquiries. Moreover, the little that admits of being said regarding the formation of these concretions may be readily inferred from the observations we have already made in reference to urinary fermentation. (See p. 412.) The analysis of these concretions falls either entirely within the department of inorganic chemistry, or will be found in the descriptions of the methods of zoo-chemical investigation, considered in different parts of this work. Those who are familiar with zoo-chemistry need hardly be referred to the copious monographs on urinary calculi with which our literature abounds. But if the practical physician should in this case, as probably in many others, be disappointed in not finding in these volumes all that he had been led to anticipate from the importance attached to the facts derived from pathologico-chemical inquiry, he must remember that the newly sown seed cannot at once blossom and bear fruit, and that years must pass before the anticipated harvest can be reaped. Truly scientific, physiological, and pathological results can only be deduced from the study of physiological processes, of which we propose to treat in our third volume.

We ought, indeed, in accordance with the entire plan of this work, to enter fully both into the consideration of the origin of the urinary constituents and the physiological importance of the urinary secretion; but we abstain from doing so, because the subjects here referred to will either be treated of in our remarks on Histo-chemistry (the chemical theory of the tissues), or fall so entirely within the department of the chemical and mechanical metamorphosis of matter, that we must defer their consideration until we enter upon the study of that subject.

END OF THE SECOND VOLUME.

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ORCHARD STREET, WESTMINSTER.

REPORT

OF

THE FIFTH ANNIVERSARY MEETING

OF THE

CAVENDISH SOCIETY.

THE Anniversary Meeting of the Cavendish Society for the year 1852 was held at the rooms of the Chemical Society, No. 5, Cavendish Square, on Monday, the 1st of March, at three o'clock in the afternoon.

The Chair was taken by THOMAS GRAHAM, ESQ., F.R.S., PRESIDENT, who called upon the Secretary to read

THE REPORT OF THE COUNCIL.

"IN reporting the result of their proceedings during the past year, the Council are again enabled to congratulate the Members on the continued prosperity and gradual extension of the Society.

"Two books have issued for 1851, namely, the first volume of LEHMANN'S 'Physiological Chemistry,' and the sixth volume of GMELIN'S 'Hand-book.' The former of these works will be completed in three volumes, the second of which is now in progress, and will constitute one of the books to be supplied to the Members this year. The sixth volume of the Translation of GMELIN'S 'Hand-book' concludes the Inorganic part of this work, in the production of which the Society has enriched the scientific literature of the country with a complete and systematic exposition of the existing state of knowledge upon the subject to which it relates. The desire to make this work generally available to British Chemists was one of the motives which originally contributed to the establishment of the Cavendish Society; and the almost unanimous approbation, which has been expressed by the Members, of the selection which the Council made of this as their first great publication, has induced them to persist in applying nearly all the means at their command towards the completion of the Inorganic part, now finished, before undertaking other works which have been in contemplation.

"In order to meet the wishes of those who may be anxious to join the Society, with the view of possessing GMELIN'S work, the Council have arranged that the sixth volume may be substituted, when desired, for the volume of 'Chemical Reports and Memoirs,' which is out of print, as one of the books for the Subscription of 1848, by which means the six volumes of the Inorganic part of the 'Handbook,' together with the 'Life of Cavendish,' may be obtained for three years' subscription, namely, 1848, 1849 and 1850. It has been arranged also that gentlemen commencing to subscribe for 1851, may have the option of taking the 'Life of Cavendish,' instead of the sixth volume of GMELIN'S 'Chemistry,' as the book which is given in addition to the first volume of LEHMANN'S 'Animal Chemistry,' for that year.

"In the last Annual Report allusion is made to a desire which had been expressed by several Members of the Society that a Translation of BISCHOF'S 'Elements of Chemical and Physical Geology' should be undertaken by the Council at as early a period as possible. The attention of the Council had previously been directed to this work, but, notwithstanding the high reputation it had acquired among scientific men, and the general interest of the subject, it was thought to be too voluminous to admit of its being undertaken while other extensive works were in hand. An arrangement has subsequently been made with the author which has removed the difficulty the Council had previously felt, and it is now decided that PROFESSOR BISCHOF shall rewrite the work for the Society in a more condensed form, and at the same time introduce such new facts and views as he may have acquired from recent observations. The preparation of this work is now in progress, and the first volume will be supplied to the Members in the course of the present year.

"The Organic part of GMELIN'S 'Hand-book of Chemistry' is also being prepared for publication."

TREASURER'S STATEMENT of the RECEIPTS and EXPENDITURE of the CAVENDISH SOCIETY, from the 1st of March, 1851, to the 26th of February, 1852.

RECEIPTS.

	£	s.	d.
Balance from previous year	407	3	11
70 Subscriptions for 1848	41	3	6
60 Ditto 1849	62	6	0
112 Ditto 1850	116	18	0
616 Ditto 1851	646	2	0
32 Ditto 1852	33	12	0
	£1307	5	5

EXPENDITURE.

	£	s.	d.
Stationery, Postage, Delivery of Books	24	15	6
Boxes for Books	10	5	3
Advertisements	1	5	6
Insurance	2	5	0
Collector's Commission	8	17	6
Secretary	85	0	0
Editorial expenses	255	0	0
Paper	212	0	0
Printing	222	13	0
Engraving and Printing Engravings	10	3	0
Binding and wrapping	134	8	5
	966	13	2
Balance in hand	340	12	3
	£1307	5	5

We have examined the above statement, and find it correct.

P. N. JOHNSON.
J. E. BOWMAN.

It was moved by Dr. John Stenhouse, seconded by Mr. Edmund Greaves, and resolved,

"That the Report just read be received and adopted."

The Meeting then proceeded to the election of Officers for the ensuing year, and the following Gentlemen were declared to have been duly elected:—

President.

Professor Graham, F.R.S.

Vice-Presidents.

Arthur Aikin, F.G.S.
Professor Brande, F.R.S.
Earl of Burlington, F.R.S.
Sir James Clark, M.D., F.R.S.
Walter Crum, F.R.S.
John Davy, M.D., F.R.S.
Michael Faraday, D.C.L., F.R.S.
J. P. Gassiot, F.R.S.
Sir. R. Kane, M.D., F R.S.
W. A. Miller, M.D., F.R.S.
Jonathan Pereira, M.D., F.R.S.
Professor Wheatstone, F.R.S.

Council.

W. R. Basham, M.D.
Jacob Bell, M.P., F.L.S.
Golding Bird, M.D., F.R.S.
J. E. Bowman, F.C.S.
P. J. Chabot, M.A., F.R.A.S.
Warren De la Rue, Ph.D., F.R.S.
W. Ferguson, F.C.S.
J. J. Griffin, F.C.S.
H. Bence Jones, M.D., F.R.S.
G. D. Longstaff, M.D., F.C.S.
T. N. R. Morson, F.L.S.
R. Porrett, F.R.S.
R. H. Semple, M.D.
W. Sharpey, M.D., F.R.S.
Charles Tomlinson, Esq.
A. W. Williamson, Ph.D., F.C.S.

Treasurer.

Henry Beaumont Leeson, M.D., F.R.S., St. Thomas's Hospital.

Secretary.

Theophilus Redwood, Esq., 19, Montague Street, Russell Square.

It was moved by MR. WILLIAM BASTICK, seconded by MR. WILLIAM GLASS, and resolved,

"That MR. T. H. HENRY, MR. TESCHEMACHER, and DR. PERCY, be appointed Auditors for the ensuing year."

The following Resolutions were unanimously adopted:—

"That the thanks of the Meeting be given to the PRESIDENT, TREASURER, and COUNCIL, for their services to the Society."

"That the thanks of the Meeting be given to the HONORARY LOCAL SECRETARIES for their services to the Society."

"That the thanks of the Meeting be given to the CHEMICAL SOCIETY for the use of their rooms on the present occasion."

The Meeting was then adjourned.

THEOPHILUS REDWOOD, SECRETARY,
19, Montague Street, Russell Square.

MARCH 1ST, 1852.

WORKS OF THE CAVENDISH SOCIETY.

1848.

1.—CHEMICAL REPORTS AND MEMOIRS. Edited by Thomas Graham, F.R.S. (Out of Print.)

2.—HAND-BOOK OF CHEMISTRY. By Leopold Gmelin. Translated by Henry Watts, B.A., F.C.S. Vol. I.

1849.

3.—HAND-BOOK OF CHEMISTRY. By Leopold Gmelin. Vol. II.

4.—HAND-BOOK OF CHEMISTRY. By Leopold Gmelin. Vol. III.

5.—THE LIFE AND WORKS OF CAVENDISH. By Dr. George Wilson.

1850.

6.—HAND-BOOK OF CHEMISTRY. By Leopold Gmelin. Vol. IV.

7.—HAND-BOOK OF CHEMISTRY. By Leopold Gmelin. Vol. V.

1851.

8.—PHYSIOLOGICAL CHEMISTRY. By Professor Lehmann. Translated by George E. Day, M.D., F.R.S. Vol. I.

9.—HAND-BOOK OF CHEMISTRY. By Leopold Gmelin. Vol. VI.

The first of the Society's publications, the volume of Chemical Reports and Memoirs, being out of print, those who now join the Society, and desire to obtain the whole of Gmelin's Chemistry, may be supplied with the first volume of this work on payment of half the Subscription for 1848; or the sixth volume of the Hand-Book of Chemistry may be substituted for the Chemical Reports and Memoirs as one of the books for 1848, so that the six volumes of Gmelin's Chemistry and The Life of Cavendish may be obtained for three years' subscription, namely, 1848, 1849, and 1850. Members commencing from 1851 have the option of taking The Life of Cavendish instead of the sixth volume of Gmelin's Chemistry as the book which is given in addition to the first volume of Lehmann's Physiological Chemistry for that year.

Honorary Local Secretaries.

Aberdeen—Dr. R. Rattray.
Banbury—Thomas Beesley, Esq.
Bath—J. P. Tylee, Esq.
Beccles—W. E. Crowfoot, Esq.
Bedford—W. Blower, Esq.
Belfast—Dr. J. F. Hodges.
Birmingham—George Shaw, Esq.
Bodmin—D. F. Tyerman, Esq.
Bolton—H. H. Watson, Esq.
Brighton—F. Busse, Esq.
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CAVENDISH SOCIETY